Cannabis use and psychotic-like experiences in two adolescent samples in Mexico City

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Cannabis Use and Psychotic-Like Experiences in Two Adolescent Samples in Mexico City

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PhD Thesis

Submitted for the degree of Doctor of Philosophy

King´s College London

I. Abstract

a. Background

Cannabis use is the most used 'illicit' drug worldwide. Prevalence of use among adolescents in Mexico has increased significantly in the last decade (Villatoro et al., 2012). Research has shown that cannabis use during adolescence may have worse adverse effects than using cannabis later in life, such as poor mental health and cannabis dependence (Gorey, Kuhns, Smaragdi, Kroon, & Cousijn, 2019). Furthermore, there has been an increased interest in the association between high potency cannabis use and its impact on psychotic-like experiences. Research has shown that highly potent cannabis use is associated with psychotic disorders (Di Forti et al., 2014). Furthermore, this association may be stronger when onset of use occurs earlier in life.

b. Aim

To identify if cannabis use predicts the appearance of psychotic-like experiences in an adolescent student sample and an adolescent substance misuse clinical sample of mainly cannabis users in Mexico City aged 15 to 19 years old.

c. Hypotheses

- Adolescent Student Sample (15 to 19 years old)
    1. Lifetime cannabis use predicts the presence of psychotic-like experiences in an adolescent student sample in Mexico City and Estado de Mexico.
    2. Frequent cannabis use predicts the presence of psychotic-like experiences in an adolescent student sample in Mexico City and Estado de Mexico.

3. Use of skunk-type cannabis vs. herbal-type cannabis predicts an increased presence of psychotic-like experiences in an adolescent student sample in Mexico City and Estado de Mexico.

- Adolescent Substance Misuse Clinical Sample (13 to 21 years old)
    1. Increased frequency of cannabis use predicts the presence of psychotic-like experiences in an adolescent substance misuse clinical sample in Mexico City and Estado de Mexico.
    2. An earlier age of first cannabis use predicts an earlier age of onset of psychotic-like experiences in an adolescent substance misuse clinical sample in Mexico City and Estado de Mexico.
    3. Skunk-type cannabis vs. herbal-type cannabis use predicts the presence of psychotic-like experiences in an adolescent substance misuse clinical sample in Mexico City and Estado de Mexico.

d. Methods

This is a cross-sectional study conducted to examine patterns of cannabis use and prevalence of psychotic-like experiences in two adolescent samples in Mexico City: an adolescent student sample, a total of 657 participants completed all the questionnaires (53% females, mean age 16.51) and an adolescent substance misuse clinical sample, a total of 121 participants completed all the questionnaires (14.8% females, mean age 16.56). Quantitative data was collected through questionnaires regarding cannabis use, psychotic-like experiences, use of other drugs and sociodemographic characteristics in

both samples. Descriptive statistics, ANOVAS, chi-square, odds ratios, linear, logistic and multinomial logistic regression analyses were conducted.

e. Results

Results are summarised by sample to facilitate identification of specific outcomes. In the student sample, no statistically significant associations were found between different patterns of cannabis use and psychotic-like experiences. In the substance misuse clinical sample, initially, daily cannabis use and use of 2 or more joints, were significantly associated with higher mean scores in the total score of psychotic-like experiences questionnaire. However, associations were no longer statistically significant whilst controlling for demographics, tobacco and use of other illicit drugs. Lastly, a significant association was found between low potency herbal type-cannabis and psychotic-like experiences (OR=.24; 95%CI=.08--.73; p=0.011) in the adolescent substance misuse clinical sample.

f. Conclusions

Overall, results from the present study are unexpected, as emerging research has shown that high potency cannabis use is associated with psychotic experiences. Although a significant association was found between herbal-type cannabis and psychotic-like experiences in the substance misuse clinical sample, this is opposite to what previous research has shown. This study has important clinical, educational and policy implications for cannabis use in adolescence.

II. Acknowledgments

This project was funded by Consejo Nacional de Ciencia y Tecnología (CONACyT). Special thanks to Centros de Integración Juvenil for their support throughout the time I was collecting data; and particularly, to all the participants who very kindly agreed to take part in this project.

I would like to express my deepest gratitude to my supervisors, Dr Michael Lynskey, for showing me that statistics are not that evil, and Dr Clare Mackie, for your constant assurance; it has been an honour working with you. Thank you for your patience and kindness throughout these 3 years.

To my father, for your endless support and always being my strength. To my mum, for your unconditional love, and to my brother, for your guidance and for being the light of my life.

Many thanks to all my PhD colleagues and friends, Carol-Ann, Erikas, Katie, Steph, John and Rob, you have made my never-ending days in the last few weeks so much better.

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IV. Figures and Tables

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V. Abbreviations and Definitions

B = Beta

CBD = Cannabidiol

CEQ = Cannabis Experience Questionnaire

CI = Confidence Intervals

CIJ = Juvenile Inclusion Centres

HR = Hazard Ratio

INEGI = Instituto Nacional De Estadística Y Geografía

M = Mean

NIDA = National Institute On Drug Abuse

OR = Odds Ratio

PICO = Population, Intervention, Comparison And Outcome

PLE'S = Psychotic-Like Experiences

QFS = Quantity By Frequency Scale

RR = Risk Ratio

SD = Standard Deviation

SE = Standard Error

SEP = Secretaria de Educacion Publica

THC = delta-9-Tetrahydrocannabinol

VI. Study Overview

a. Introduction

The potential association between cannabis use and psychotic-like experiences, and the origins of any association, have been an important field of research during the past two decades. Studies have shown that frequent cannabis use is an important contributor to

the development of psychotic-like experiences (PLE's) (Di Forti et al., 2015) and, research has shown that the earlier the age of first use, the higher the probability of developing psychotic-like experiences (Fergusson, Horwood, & Swain-Campbell, 2003). Research has shown that adolescence is a crucial phase in human development, both physical and neurological (Wright & Kutcher, 2016) and substance use at this stage in life has more detrimental educational and cognitive repercussions than use later in life (Casadio, Fernandes, Murray, & Di Forti, 2011). However, most research has been conducted in Europe or the United States of America, and there is need for replication in different populations and different countries.

In addition, surveys have shown that the prevalence of cannabis use among adolescent students has steadily increased since 2006 (Villatoro et al., 2015). Studies to identify the repercussions cannabis use has in adolescent populations are needed to support and assist in the development of public policies. Studies regarding cannabis use and psychotic-like experiences have been conducted in developed countries, for example the United Kingdom (Mackie et al., 2013) and United States of America (Bechtold, Hipwell, Lewis, Loeber, & Pardini, 2016). However, research in developing countries, including Mexico, is largely absent from the literature, and essential.

Furthermore, since 2016, Mexico has undergone major debates about changing policy regarding cannabis (SEGOB, 2016) and recently, the Senate discussed changing legalization and proposed a reform of the current laws around possession, cultivation and licensing (Republica, 2020).

b. Rationale

Cannabis use in adolescents has been shown to increase the risk of developing psychotic like experiences. Studies have been conducted in both, adolescent general population (Kuepper et al., 2011; Miettunen et al., 2008) and adolescent clinical settings (substance users) and in both, the risk of presenting these experiences increase with cannabis use (Hodgins, Larm, & Westerman, 2016). The present study aims to identify if cannabis use predicts the appearance of psychotic-like experiences in two adolescent samples in Mexico. Participants were recruited from a school and a substance misuse clinical sample of young people seeking treatment for cannabis related problems. To the best of my knowledge this is the first study examining cannabis use and psychotic-like experiences in adolescent population in Mexico City. Due to fundamental differences between samples, data will not be combined for analysis; instead each set of data will be analysed individually to identify and observe the outcomes of each individual sample.

c. Research Questions

- Adolescent Student Sample (15 to 19 years old)
    1. Does lifetime cannabis use predict the presence of psychotic-like experiences in an adolescent student sample in Mexico City?
    2. Does frequent cannabis use predict the presence of psychotic-like experiences in an adolescent student sample in Mexico City?
    3. Does the use of skunk-type cannabis vs. herbal-type cannabis predict an increased presence of psychotic-like experiences in an adolescent student sample in Mexico City?

- Adolescent Substance Misuse Clinical Sample (13 to 21 years old)

    1. Does increased frequency of cannabis use predict presence of psychotic-like experiences in an adolescent substance misuse clinical sample in Mexico City?

    2. Does an earlier age of first cannabis use predict an earlier age of onset of psychotic-like experiences in an adolescent substance misuse clinical sample in Mexico City?

    3. Does skunk-type cannabis vs. herbal-type cannabis use predict presence of psychotic-like experiences in an adolescent substance misuse clinical sample in Mexico City?

d. Aim and Objective

The aim of the present study is to identify if cannabis use predicts the appearance of psychotic-like experiences in an adolescent student sample 15 to 19-year olds and an adolescent substance misuse clinical sample of mainly cannabis users in Mexico City aged 13 to 21-year olds.

VII. Chapter Overview

Chapter 1. Introduction: Cannabis Use History, Prevalence, Pharmacology and Effects

Chapter One portrays an introduction to history of cannabis use worldwide and particularly in Mexico. This is followed by comparisons between the United States of

America, the United Kingdom and Mexico regarding prevalence of use. Lastly, a review of the known effects of cannabis in adolescents and how cannabis has been associated with psychotic-like experiences, symptoms and disorders.

Chapter 2. Cannabis Use and Psychotic-Like Experiences in Adolescents: A Systematic Review

Chapter Two shows the results of a systematic review conducted in all available research on cannabis use and psychotic-like experiences in adolescents. Systematic reviews have been previously conducted in the subject among adult population, however, never for adolescents. Results are summarized by patterns of cannabis use and an extensive and in-depth table with all relevant information of each study can be found in the Appendix.

Chapter 3. Methodology

The third chapter comprises the full description of the methodology used throughout the study. It also contains a summary of the school system in Mexico, of the boroughs attended and of the organization that was contacted in order to conduct data collection. The recruitment and sampling strategies are described along with detail about the questionnaires used for data collection and their background. Lastly a small description of each sample is given.

Chapter 4. Patterns of Cannabis Use and Associated Factors in an Adolescent Student Sample in Mexico City

Chapter Four provides a detailed description of the constructs assessed regarding cannabis use. Patterns of cannabis use are fully depicted (lifetime, frequency, quantity, type of cannabis mainly used, method of use and social vs. non-social use), alongside associated factors (age, gender, ethnicity, socioeconomic level and cannabis experience questionnaire). Psychometric properties of the cannabis experience questionnaire are presented.

Chapter 5. Cannabis Use and Psychotic-Like Experiences in an Adolescent Student Sample in Mexico City

Chapter Five describes the psychometric properties of the PRIME Screen Questionnaire. It also describes the prevalence of psychotic-like experiences in the student sample, the associations with sociodemographic characteristics, patterns of cannabis use and use of other drugs.

Chapter 6. Cannabis Use and Psychotic-Like Experiences in an Adolescent Substance Misuse Clinical Sample in Mexico City

Chapter Six provides the rationale behind the examination of cannabis use and psychotic-like experiences in an adolescent substance misuse clinical sample, the associations between cannabis use and use of other drugs, the associations between use of other drugs and psychotic-like experiences and the associations between patterns of cannabis use and psychotic-like experiences bivariate and full adjusted models.

Chapter 7. Discussion

This final chapter will provide an overview of the results of the present study along with different hypotheses to explain those results. The chapter will conduct a thorough examination of similarities and differences between the present study and research conducted previously.

1. Introduction: Cannabis Use: Prevalence, History, Pharmacology and Effects

The focus of this chapter is an examination of cannabis; antecedents of use, its pharmacodynamics and pharmacokinetics, prevalence of use and adverse effects. Furthermore, a review of the literature available on adolescent cannabis use and adverse effects during this period of life is provided below. Lastly, a brief summary of research on cannabis use and how it may contribute and increase the risk to develop psychotic-like experiences is provided as an introduction to Chapter 2, Cannabis Use and Psychotic-Like Experiences in Adolescents: A Systematic Review.

1.1. Cannabis History

It has been difficult to determine with complete certainty the origins of cannabis, however some of the first traces of cannabis sativa date back more than 4,000 years. These first traces were found in China and the surrounding area. It was mainly used with medicinal purposes and to manufacture textiles (Russo, 2007). The first documented records were found in north-eastern Asia around 2,700 B.C., when it was mainly used as an analgesic, muscle relaxant, antidepressant, hypnotic, anti-inflammatory among others (Aggarwal, 2009; Zuardi, 2006). Cannabis comes from a complex family of *cannabaceae*, where different types of cannabis can be found; for example, *cannabis sativa*, *cannabis indica* and *cannabis ruderalis* (Russo, 2007). Furthermore, from these types of cannabis different preparations for its use can be found, depending of method of use. For smoked cannabis preparations are normally, herbal cannabis, also known as marijuana or grass, sinsemilla, also known as skunk, and hashish (Russo, 2007). However, other preparations can now be found, like vaporizers,

concentrates and edibles which, after cannabis legalisation in parts of the United States of America, have become more prevalent in some states (UN, 2019a).

1.2. Cannabis Psychopharmacology

A breakthrough in cannabis pharmacological research occurred in 1964 when Gaoni and Mecholuam identified delta-9-tetrahydrocannabinol (THC) as the main active ingredient in cannabis sativa (Meyer & Quenzer, 2013; Wright & Kutcher, 2016). This is only one of the at least 143 unique cannabinoid compounds that can be found in cannabis. Research has shown that THC is the principal component that provides the psychoactive effects or the feeling of "high", for example euphoria and disinhibition (Bloomfield et al., 2019). The second most important compound, which has been subject to extensive research is cannabidiol (CBD), which is known for its non-psychoactive effects and, it has also been shown to counteract the effects produced by THC (Bloomfield et al., 2019).

Research has shown that each preparation has different characteristics and different levels of THC and CBD. Recently, a study that examined the changes in potency (concentration of delta-9-tetrahydrocannabinol) in cannabis resin and herbal cannabis across Europe found an increase in potency in resin from 8.14% in 2006 to 17.22% in 2016; furthermore, potency observed in herbal cannabis increased from 5% in 2006 to 10.22% in 2016 (Freeman et al., 2018).

Cultivation processes have been continuously changing, from outdoor cultivation to more recently, indoor cultivation, which usually involves the use of controlled growing conditions and selective breeding. These controlled conditions and selective breeding focus on altering the quantity of different compounds found in the plant and increase levels of THC to increase the desirable effects of users.

Furthermore, a program at the University of Mississippi in the United States of America (USA), alongside the National Institute on Drug Abuse (NIDA) have been continuously monitoring the potency of USA cannabis preparations. Cannabis samples are obtained from confiscated samples and then classified in different categories, depending on its characteristics. Categories are as follows: cannabis, hashish and hash oil; cannabis is then categorised as marijuana or sinsemilla. Analyses over the last decade have shown a significant increase in delta-9-tetrahydrocannabinol concentrations from 8.9% in 2008 to 17.1% in 2017 (Chandra et al., 2019). Examination of mean delta-9-THC:CBD ratio across time also showed a considerable increase, from 23 in 2008 to 104 in 2017. To the best of my knowledge, no research has been conducted in Mexico to identify different levels of concentrations of THC or CBD in cannabis. However, research worldwide in recent years has shown that CBD concentrations continue to decrease, whereas THC concentration levels continue to increase.

Burning of cannabis, which is the most prevalent method of use, causes THC to vaporise and enter the user's lungs in small particles. The amount of THC absorbed is affected by the amount used and by the pattern of smoking, which means that the effects are influenced by puff volume, frequency, inhalation depth and breath-hold duration

(Onaivi, 2006). THC is rapidly absorbed through the lungs, resulting in increasing levels of THC in blood plasma, once peak levels have been reached, THC levels in plasma start to decline fairly rapidly as a result of metabolism in the liver and accumulation of cannabis in fat cells in the body. However, complete elimination is much slower because of the persistence of the drug in fat tissue. Overall, elimination rate is from 20 to 30 hours, nevertheless due to its storage in fat cells, urine screening for THC can result positive even after 2 weeks after a single use of cannabis. Even when there are other methods of use, the most prevalent one is by smoking.

1.3. Endogenous Cannabinoid System

The pharmacological characterization of a central nervous system cannabinoid receptor was announced in 1988 by a group of researchers at the Pfizer pharmaceutical company (Meyer & Quenzer, 2013). Research followed and showed that the cannabinoid receptor was significantly expressed in many brain regions including the basal ganglia, hippocampus, cerebellum and cerebral cortex, which is consistent with the visible effects cannabis has on coordination, memory and locomotor activity (Glass, Dragunow, & Faull, 1997). Cannabinoid receptor named as CB_{1R}, can be found at high concentrations in specific brain regions linked with cognitive and emotional processing and rewards (Bloomfield et al., 2019). Later, another cannabinoid receptor was identified and named as CB_2, which can be found in bones, gastrointestinal tract, fat cells and in the immune system (Meyer & Quenzer, 2013).

Cannabinoid receptors belong to the family of metabotropic receptors, second messengers, they exert their effects by coupling to G-proteins. Effects involve inhibition

of cAMP (cyclic adenosine monophosphate), voltage sensitive Ca^{2+} (calcium) channels and activation of K^{+} (potassium) channel opening. Cannabinoid receptors can also influence gene expression through a complex system of protein kinases known as the mitogen-activated protein kinase (MAPK) system. CB_1 receptors have been found on the axon terminal instead of the postsynaptic cell, and by activating presynaptic receptors cannabinoids can inhibit the release of different neurotransmitters, for example serotonin, glutamate, dopamine, norepinephrine, acetylcholine and GABA (gamma aminobutyric acid) (Iversen, 2003). Research has shown that THC acts as a partial agonist rather than a full CB_1 and CB_2 receptor agonist. In addition to THC, cannabis' leaves usually contain more than 143 other types of cannabinoids (Hanus, Meyer, Munoz, Taglialatela-Scafati, & Appendino, 2016). Cannabidiol has been shown to have therapeutic effects on the treatment for epilepsy, anxiety, psychosis and addictions (Bloomfield et al., 2019).

1.4. Cannabis Use in Mexico

Records show that hemp (one of the strains belonging to the cannabis sativa family) was first introduced in Mexico in the fifteenth century, during the Spanish conquest, by mandate of the Spanish Crown who ordered its cultivation in the country (Campos, 2012). Hemp was widely used by the Spanish as a source of fabric to produce various goods, for example ropes and sails used in the navy, therefore the interest of the crown to produce and manufacture it. Although its use was firstly meant for textile production, it was not long before people working in the fields realised the potential medicinal use of hemp (Campos, 2012). Cultivation started in different parts of Mexico; however, as people were not familiar with the process of growing hemp, instructions had to be provided and it took time for people to learn. For two hundred years hemp was seen

only as a fibre from which textiles could be produced, however in the 1760's approximately, locals around Mexico City started using different preparations of hemp for different purposes and, as a result, people started viewing it as an indigenous drug. This marks the start of the prohibitionist view in Mexico and the reason cannabis started to be seen as something that could provoke disorder and madness. All of this provides an overview of how cannabis was firstly introduced in Mexico and the relationship people in the country developed with it. Cannabis was then banned in 1920 in Mexico by sanitary authorities. Seventeen years later the United States of America passed the first legislation to control cannabis sales.

1.5. Prevalence of Cannabis Use: Comparison between the United Kingdom, United States of America and Mexico

Cannabis is the illegal drug most commonly used worldwide, with approximately 188 million lifetime users (UN, 2019a). From 1998 to 2007, global prevalence of lifetime cannabis use increased from 3.4% to 3.9%. During the last decade it has remained relatively stable. On the other hand, past year cannabis use has shown an estimated increase of roughly 30% from 1998 to 2017 (UN, 2019a). Furthermore, past year cannabis use has been seen to increase in Canada and in the United States of America; with 7% of the population aged from 15 to 64 in 2007 reporting past year use to 8.4% in 2017, with the highest increase observed in the United States (UN, 2019a). Epidemiological research in the United States on substance use show that lifetime cannabis use among adults increased 10% from 2002 to 2017; furthermore, past year use increased 50% and monthly cannabis use increased 65%. Lastly, data show that daily or nearly daily use has doubled particularly over the past decade (CBHSQ, 2017).

Regarding adolescent cannabis use in the United States of America, data from the most recent publication of the report Monitoring the Future conducted among 8th, 10th and 12th graders showed that lifetime cannabis use has remained relatively stable among adolescents in the past decade with 27.9% reporting ever use in 2008 to 29.7% in 2018. Moreover, past year cannabis use has shown a slight increase from 21.5% of adolescents reporting use in the last 12 months in 2008 to 24.3% in 2018; lastly, prevalence of past month cannabis use went form 12.5% of adolescents reporting use in the past 30 days in 2008 to 14.6% in 2018 (Johnston et al., 2019).

In the United Kingdom, prevalence of lifetime cannabis use was 30% among 16 to 59-year olds. Furthermore, it was found that 7.2% of adults (16 to 59 years old) reported past year use of cannabis, and among 16 to 24-year olds 16.7% reported past year cannabis use. Overall, data have shown that cannabis use has decreased among both groups in the past 20 years (Flatley, 2018).

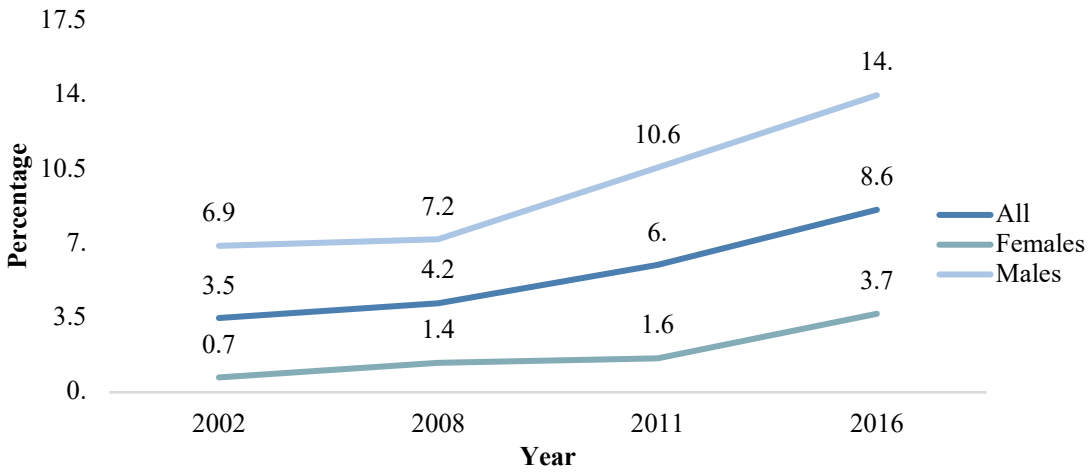
1.5.1. Prevalence of Cannabis Use in Mexico

The most recent national report on drug use in Mexico was published in 2017, results showed that cannabis is the illegal drug most widely used in the country, with a prevalence of lifetime use of 8.6% in the general population. Overall, research has shown that cannabis use has increased in Mexico, particularly in the past few years (Villatoro, 2017). Prevalence of use at least once (lifetime use) in 2016 was 8.6% among general population (age range of 12 to 65 years old), which has more than doubled since the year 2002 when prevalence of ever use among the general population was of 3.5%. Furthermore, when examining prevalence of lifetime cannabis use by

gender it can be observed that the increase among females has been greater, with an increase of more than five times, showing 0.7% in 2002 of women reporting ever use of cannabis compared to 3.7% in 2016 (Villatoro, 2017); whereas in men, prevalence of use doubled from 6.9% in 2002 to 14% in 2016 (Figure 1.1). Research has shown that prevalence of cannabis use in the past year in Mexico has increased, with 0.6% reporting past year use in 2002 to 2.1% in 2016. Furthermore, past month cannabis use has also been shown to increase, with 0.8% reporting use in the last month in 2011 to 1.4% in 2016 (Villatoro, 2017).

Figure 1.1 Lifetime Cannabis Use in General Population in Mexico

(12 to 65 Year Olds)

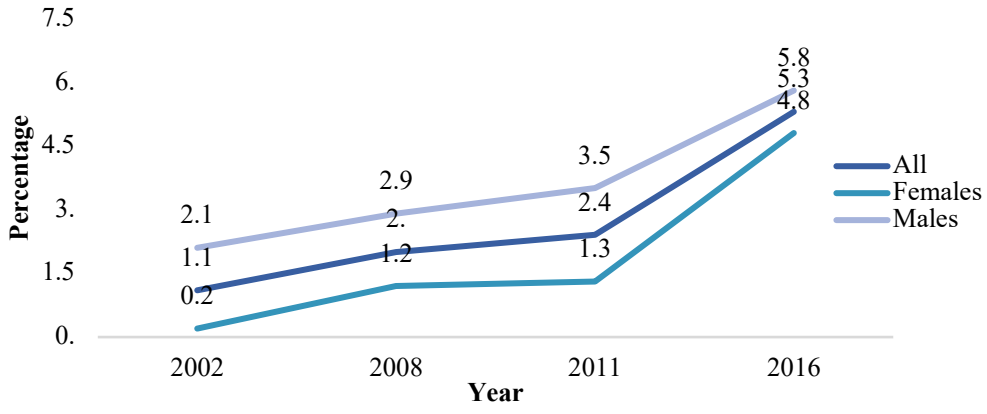


Even when cannabis continues to be the most prevalent illegal drug used worldwide, when comparing its prevalence of use among similar populations in different countries, for example Mexico and the United Kingdom; it can be observed that prevalence of use varies. In the United Kingdom, even when cannabis is a widely used drug, its

prevalence of use does not seem to be increasing (Flatley, 2018). This is not the case in Mexico, as stated above; prevalence of cannabis use among the general population and particularly among females continues to increase

To date, there has been limited published research on patterns of cannabis use and potential harmful effects in Mexico. Nonetheless, available epidemiological evidence suggests that a substantial number of adolescents in Mexico use cannabis and that the prevalence of use is increasing. In the report previously mentioned from Villatoro et al., data collected from adolescents from 12 to 17 years old in Mexico indicates that lifetime cannabis use is rapidly increasing. In 2002 only 1.1% of adolescents in the country reported lifetime cannabis use, whereas in 2016 this number increased to 5.3% (Figure 1.2). Furthermore, female cannabis use in this age range had a major increase going from 0.2% of lifetime users in 2002 to 4.8% in 2016 (Villatoro, 2017).

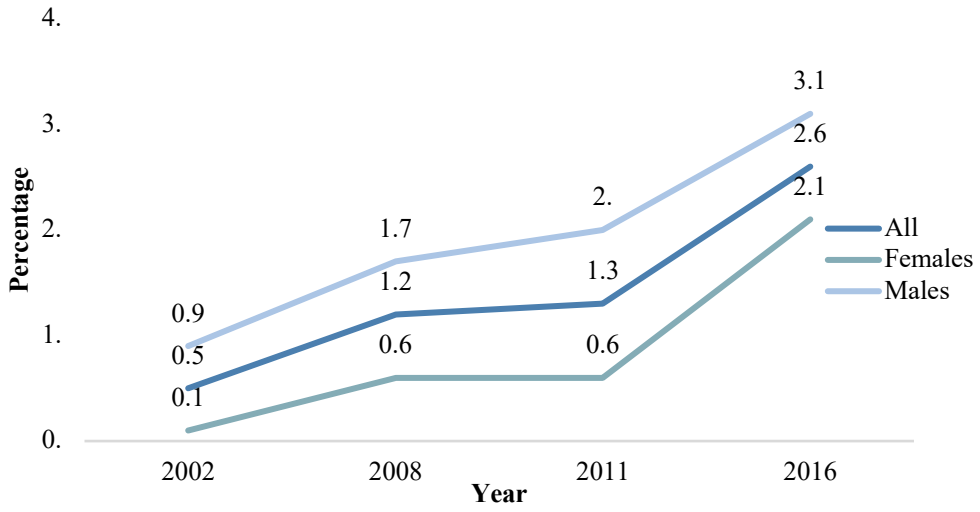
Figure 1.2 Lifetime Cannabis Use in Adolescents in Mexico (12 to 17 Year Olds)



Past year cannabis use has also shown a significant increase in the past decade among adolescents (12 to 17-year olds) in Mexico, particularly in the past 5 years (Figure 1.3).

Prevalence of past year use in 2002 was 0.5% among adolescents, however, recent data show a significant increase, with 2.6% of adolescents reporting cannabis use in the past year (Villatoro, 2017). According to gender, and as observed in lifetime cannabis use, females show a higher increase in prevalence of use, with only 0.1% of participants reporting past year cannabis use in 2002 compared to 2.1% in 2016 (Figure 1.3).

Figure 1.3 Past Year Cannabis Use in Adolescents in Mexico (12 to 17 Year Olds)



1.5.2. Cannabis Use in Adolescents in Mexico City

Mexico City is the largest city in Mexico, with a total population of 8,918,653 (INEGI, 2017a). Prevalence of lifetime cannabis use in Mexico City among the general population in 2016 was 9.1%, and past year cannabis use was 2.5% (Villatoro, 2017). A survey among adolescent students from 13 to 19 years old in Mexico City found that the prevalence of use of any illegal drug in 2014 was 26.6% and the average age of initiation reported was 13.5 years old (Villatoro et al., 2015). Furthermore, 19.6% of

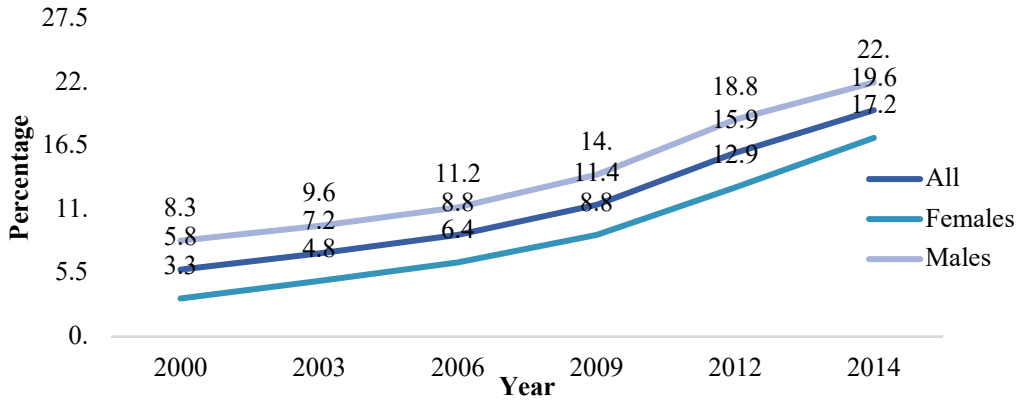
adolescent-students (13 to 19-year olds) in the city reported using cannabis at least once in their lifetime in 2014 (Villatoro et al., 2012; Villatoro et al., 2015).

As shown in

Figure 1.4 an increasing trend has been observed in the prevalence of cannabis use in the adolescent population in Mexico City. From 5.8% of adolescents reporting ever use of cannabis in 2000 to 19.6% in 2014. With the most pronounced increase shown from 2006 with 8.8% of adolescents reporting lifetime use to 19.6% in 2014. When examining ever use of cannabis by school grade (secondary school and high school) in 2014, results showed that 9.8% of adolescents in secondary school reported lifetime cannabis use, compared to 30.1% of adolescents in high school. Results indicate that adolescents in high school are more likely to have used cannabis at least once in their lifetime than adolescents in secondary school, probably due to age and easier availability.

Figure 1.4 Lifetime Cannabis Use in Adolescents in Mexico City

(13 to 19 Year Olds)



When examining differences in lifetime cannabis use by gender, results showed that males are more likely to use cannabis, results indicate an average of 5 points higher prevalence of cannabis use in males than in females. Nevertheless, a significant increase in cannabis use among females was seen from 2012 to 2014, with a prevalence of use of 12.9% to 17.2% respectively, which indicate that adolescent females are being more prone to experiment with cannabis in recent years than previously. Similar trends have been identified in other reports such as the World Drug Report, where data show significantly higher prevalence of use among males in Canada than females (UN, 2019b).

Apart from lifetime cannabis use, students from 13 to 19 years old had to report cannabis use in the past year. Results showed a significant increase from data in 2009 to 2014, with 8.2% of students reporting past year use of cannabis compared to 14.2% respectively. Overall, results show significant difference in prevalence of past year cannabis use in 2000 with 3.4% compared to 14.2% in 2014 (Villatoro et al., 2015). As

previously observed in lifetime prevalence of cannabis use among females, a significant increase in past year prevalence of female cannabis use was reported with 6.2% in 2009 to more than double in 2014 with 12.7% (Villatoro et al., 2015).

Figure 1.5 Past Year Cannabis Use in Adolescents in Mexico City

(13 to 19 Year Olds)

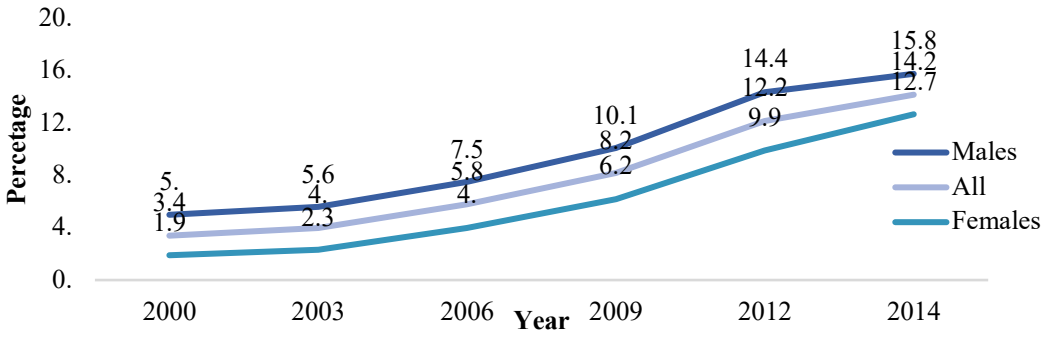
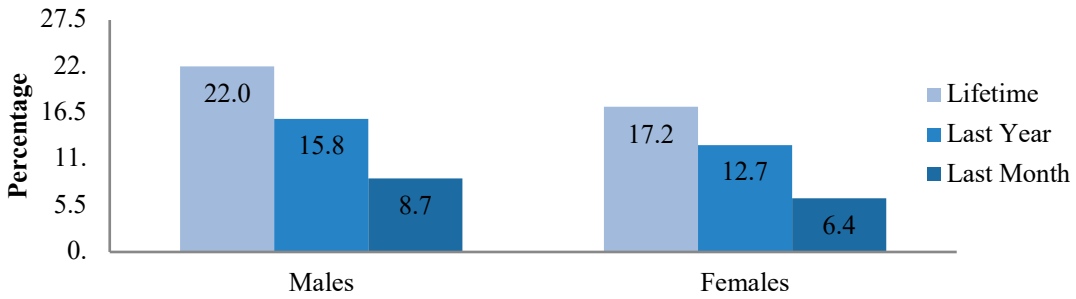


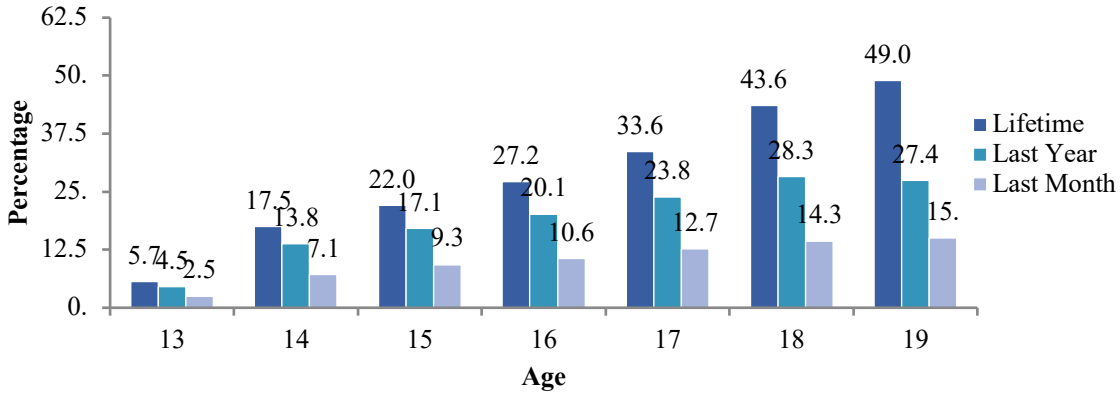
Figure 1.6 Cannabis Use in Adolescents in Mexico City According to Gender in 2014

(13 to 19 Year Olds)



Furthermore, results by gender on lifetime, last year and last month cannabis use are shown in Figure 1.6. Throughout, it can be observed that prevalence of use is higher among males than females, particularly in ever use, however, monthly use show a minor difference in comparison with the other types of measurements, with 8.7% of males reporting monthly use compared to 6.4% of females.

Figure 1.7 Cannabis Use According to Age in Adolescents in Mexico City in 2014

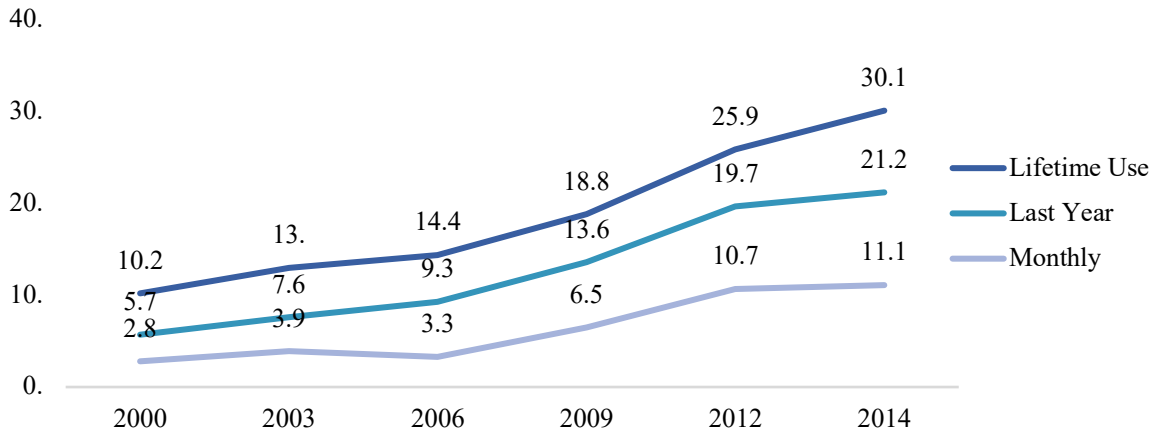


It can be observed that cannabis use was more common among adolescents from 16 to 19 years old; ranging from 27.2% lifetime use in 16-year olds to almost half of 19-year olds having used cannabis at least once in their life (Figure 1.7). The following data on prevalence of use will focus on adolescents aged from 16 to 19 years old.

1.5.3. Cannabis Use in Adolescents from 16 to 19 Years Old in Mexico City

The main interest of the present study and the age range of the population recruited and analysed were adolescents from 15 to 19 years old. As shown in Figure 1.7, previous reports have shown that prevalence of use in Mexico City among adolescents aged 16 to 19 years old is higher than earlier in life (Villatoro et al., 2015).

Figure 1.8 Cannabis Use in Adolescents from 16 to 19 Years Old in Mexico City



Prevalence of lifetime cannabis use has tripled since 2000, with 30.1% of adolescents reporting ever use of cannabis in 2014, compared to 10.2% in 2000 (Figure 1.8). Furthermore, adolescents reporting use of cannabis in the last year increased from 5.7% in 2000 to 21.2% in 2014, showing a significant increase recent use of cannabis than previously. Similarly, monthly cannabis use has increased significantly, with 2.8% of adolescents in 2000 reporting frequent use compared to 11.1% in 2014. These results indicate that cannabis use among adolescents in Mexico City continues to increase, and with this increase of prevalence of use, health and mental risk factors may do as well. Moreover, debates in Mexico regarding plausible legalisation started to emerge in Mexico (SEGOB, 2016), therefore, evidence about cannabis use and its adverse effects is paramount. In the following sections I will discuss research conducted in other countries regarding cannabis use, adverse effects and psychotic-like experiences.

1.5.4. Cannabis Use During Adolescence

Adolescence is a significant period of human development. During adolescent years physical, emotional, social and neurocognitive changes take place, influenced by genetic and environmental factors, which interact and impact on the development and behaviour of the individual (Wright & Kutcher, 2016). The World Health Organisation defines adolescents as people between the ages of 10 to 19 years old; youth is defined by the United Nations as 15 to 24-year olds; and young people as 10 to 24 years old (UN, 1989). Substance use during these years could have potential long-term consequences; therefore, the importance of the present study. For the purpose of the present study, the age range used for the term adolescence is 10 to 24 years old.

Research has shown that the endocannabinoid system is involved in brain development during adolescence. Continued use of cannabis may alter the normal development process (Lubman, Cheetham, & Yücel, 2015) and have short- and long-term consequences, for example disturbance in prefrontal development and disinhibition of prefrontal function (lack of impulse control) (Miller & Cohen, 2001) . Furthermore, frequent and heavy cannabis use has been associated with different cognitive impairments, for example memory and learning (Medina et al., 2007) response perseveration (recurrence of a response without the appropriate stimuli) (Allison, 1966; Lane, Cherek, Tcheremissine, Steinberg, & Sharon, 2007) and attention (Harvey, Sellman, Porter, & Frampton, 2007).

A longitudinal study following 1,037 participants from birth to adult life, assessing neuropsychological performance found that participants using cannabis weekly or that

were diagnosed with cannabis dependence prior to 18 years old showed higher deterioration in full scale of IQ than participants without weekly use or that were diagnosed later in adulthood. Among adolescent onset, heavy user's impairment remained even after one or more years of abstinence (Meier et al., 2012). A systematic review found that executive functions are generally more impaired in regular cannabis users, compared to adults and that age dependent effects may be more pronounced in dependent and heavy users (Gorey et al., 2019). Research has found that during adolescence some risk behaviours are correlated with cannabis use, abuse and sometimes problematic use to the point of dependence, for example, smoking and some antisocial behaviours (Coffey & Patton, 2016).

1.5.5. Adverse Effects of Cannabis Use

Cannabis effects can be divided into acute or chronic. Acute effects are those experienced immediately after use, that is while intoxicated, and can include anxiety, paranoia and dysphoria as well as psychomotor impairment particularly when driving (Silverman et al., 2015). Moreover, a review of the existing literature found that when used daily or almost daily, cannabis may have worse adverse long-term consequences in health and social life. Some of these adverse consequences include attention and memory deficits, and risks of mental health problems including depression and psychotic-like experiences (Hall, 2014).

A longitudinal birth cohort study examined the relationship between adolescent cannabis use and tobacco use by age 15 and later educational outcomes. Results showed that tobacco and cannabis use at age 15 were significantly associated with later negative

educational outcomes at 16; effects remained after adjusting for various covariates (Stiby et al., 2015). Furthermore, a study that examined data from three cohort studies in three Australasian samples found that participants that did not use cannabis before 18 years old were up to four times more likely to complete high school (OR=3.6; 95%CI= 1.6-2.2), up to three times more likely to be enrolled in an university (OR=2.3; 95%CI= 1.8-3.1) and almost five times more likely to have complete an university degree (OR=3.7; 95%CI= 2.8-4.9) (Horwood et al., 2010). These results, alongside a previous review conducted on adolescent cannabis use and educational attainment (Lynskey & Hall, 2000) show that cannabis use during adolescence may have detrimental effects in attaining good educational outcomes. However, studies have also shown that the strength of the association between cannabis use and detrimental effects on cognition is weak (Gorey et al., 2019).

Moreover, cannabis use has been shown to impact mental health. A longitudinal study examined if adolescent cannabis use and tobacco at age 16 increased the risk of depression at age 18 and found that after adjustment for pre-birth and childhood confounders the effect of the relationship was attenuated but persisted for cannabis use (OR= 1.38; 95%CI= 1.09-1.75; p=.007) (Gage et al., 2015). Furthermore, a systematic review conducted in 2007 which examined cannabis use and the risk of psychosis or other type of mental health problems, e.g. affective symptoms, found that ever use of cannabis increased the risk of presenting any type of psychotic symptom or disorder (OR=1.41; 95%CI= 1.20-1.65). The risk increased when frequency of cannabis use was higher (OR=2.09; 95%CI= 1.54-2.84) showing a dose-response effect, where the more frequent cannabis use, the higher the risk of psychotic outcomes (Moore et al., 2007).

Occasionally, cannabis may not be perceived as a harmful drug, as users claim it is – natural- and that given the absence of "harmful chemicals" in it the risk of using is small or non-existent (McGinty, Niederdeppe, Heley, & Barry, 2017). Nevertheless, research has shown that cannabis can have harmful effects in users (Hall, 2014). Furthermore, modifications in concentrations made in cannabis are a matter of concern as this increases its potency and in consequence increases the risk of developing short- and long-term harms, for example psychotic-like experiences.

1.6. Psychotic-Like Experiences

1.6.1. History of Psychosis

The term "psychosis" was first created in 1845, and initially it encompassed a number of different mental disorders. Firstly used in Germany by Feuchtersleben who coined the term "psychosis" and "psychopathy", believed that these disorders were "diseases of the personality" and that these were caused by a different combination of factors, both physical and "psychic", and that these affected the person as a whole (Beer, 1996). Furthermore, both terms were a different form to call "insanity". The term ´psychosis´ when viewed from the Greek structure translates as follows: psyche translates as soul or life, and in a more modern terminology it means "mind". The suffix "-osis" means "any illness of" which in conjunction, psychosis means "any illness of the mind" (Beer, 1996). Initially it can be observed by the way authors used the term that psychosis and psychopathy, both referred to any type of mental disorder. It was only later, that distinctions had to be made in order to distinguish between the different types of mental

disorders. In the early nineteenth century, even the psychiatrist Alzheimer used psychosis interchangeably with other types of mental disorders (Beer, 1996).

1.6.2. Psychotic-Spectrum Disorders

To understand further the interest in the development of psychotic-like experiences, it is important to know what these experiences are and the repercussions they have in daily life functioning. Currently, psychosis is identified as only one end of the psychotic-spectrum disorders, which can occur due to different medical, psychiatric or neurological conditions and, schizoid personality disorder to be in the other end (Arciniegas, 2015). It is important to remember that these are disorders, both in the extreme end of the psychosis continuum, which is addressed below. Prodromal symptoms are described as tenuous, subclinical symptomatology that does not meet criteria for a full psychotic diagnosis and these symptoms have been found to appear prior to the formal clinical diagnosis of a psychotic disorder (Bagot, Milin, & Kaminer, 2015).

Difficulties arise from trying to differentiate terms that frequently have been used interchangeably to explain psychotic symptoms or psychotic-like experiences. A systematic review conducted in 2016 on definitions and assessments of psychotic-like experiences found that the following terms have been used to refer to “psychotic-like experiences”: schizotypy traits, magical ideation, unusual experiences, anomalous experiences, hallucinatory experiences, delusional-like experiences, psychotic or psychosis-like experiences and subclinical psychotic symptoms (Lee et al., 2016). These findings show the lack of agreement and the variability which researchers and clinicians face when assessing these symptoms or experiences.

Psychotic-like experiences are symptoms observed in psychotic disorders, for example in schizophrenia or brief psychotic disorder. These symptoms or experiences can be distortions of thought and perception, including hallucinations (visual, auditory or tactile), delusions and thought disorders (WHO, 2016). Someone experiencing a psychotic episode might find it difficult to distinguish what is real from what is not. Other symptoms that may appear during a psychotic episode are anxiety, depression, social inadequacy, lack of motivation and problems functioning in day to day life (CBHSQ, 2017).

1.6.3. Subclinical Psychotic-Experiences in the General Population

Recently, it has been found that these experiences or symptoms are not only found in patients with diagnosed psychotic disorders, but also in the general population (Kelleher et al., 2012). A systematic review and meta-analysis conducted in 2009 examining psychotic experiences as a continuum showed prevalence rates from 5% to 8% in general population (van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009). Results indicate that the clinically diagnosed psychoses represent only a small proportion of the continuum and that non-clinical psychotic-like experiences are more common than previously thought. Furthermore, providing that people in this proportion of the continuum are also using cannabis, which by its own has shown to increase the risk of developing psychotic-like experiences, they could be at risk of an increased presence of psychotic-like experiences or worsening of symptoms (Griffith-Lendering et al., 2013). Another example of this type of continuum is blood pressure and glucose, these are continuously present in the general population however, medical terms like

hypertension and diabetes exist to explain the extreme of the continuous, that is the clinical cases of the continuum; which in this case, would be a diagnosis of a psychotic disorder (Van Os, 2001).

1.6.4. Cannabis Use and Psychosis or Psychotic-Like Experiences

One of the first epidemiological studies showing evidence of an association between cannabis use and psychosis, more specifically, in-patient admission for schizophrenia, was conducted in 1987 by Andréasson et al. in a Swedish cohort of 45,570 male conscripts (age range 18 to 21-year olds). Results from extracted data showed that conscripts that had used cannabis over fifty times, had six times higher risk of developing schizophrenia than non-users (CI 95%, 4.0 – 8.9) (Andreasson, 1987). Since then, the association between cannabis use and psychotic-like experiences has been a matter of continuing scientific interest; a longitudinal study of a New Zealand birth cohort examined the risk for developing schizophreniform disorder and schizophrenia symptoms in adolescent cannabis users studied from age 11 to 26-years (Arseneault et al., 2002). Whilst controlling for psychotic symptoms at 11, logistic regressions showed that cannabis users at 15 were four times more likely to develop a schizophreniform disorder at age 26 than individuals who had never used cannabis.

Fergusson et al. in 2003, reported the results of a longitudinal study that examined the links between cannabis dependence (DSM-IV criteria) at ages 18 and 21 and rates of psychotic symptoms, assessed by using items from the Symptom Checklist 90 (SCL-90). Results showed that cannabis dependent users at age 18 had 3 to 7 times higher rates of psychotic symptoms than non-cannabis dependent users. At age 21 cannabis

dependent (DSM-IV criteria) participants showed 2 to 3 times higher rates of psychotic-symptoms than non-dependent participants. The association remained significant (RR=1.8; 95%CI= 1.2-2.6) after the adjustment of confounding factors such as other substance use, anxiety and depression (Fergusson et al., 2003). Substance use, apart from cannabis, has been continuously and persistently associated with psychotic-like experiences and it has been shown to be a significant risk factor for the later development of psychotic disorders (Fonseca-Pedrero, Lucas-Molina, Perez-Albeniz, Inchausti, & Ortuno-Sierra, 2019; Levy & Weitzman, 2019; Mackie et al., 2013).

Furthermore, in 2016, Marconi et al. conducted a meta-analysis exploring levels of cannabis use and risk of psychosis, of all published data including general population and first episode psychosis patients, reporting a consistent and strong association between the amount of cannabis used and the risk for psychosis. The studies included in the meta-analysis assessed use of cannabis exploring frequency, amount and severity prior to the onset of psychosis and psychotic related data established with validated measures. They found a four-fold increased (OR = 3.9, CI 95%, 2.8 – 5.34; unadjusted) risk in participants with more severe cannabis use (daily use/cannabis dependence) and a two-fold increase for the average (year/monthly use) cannabis user in comparison to non-cannabis users (Marconi, Di Forti, Lewis, Murray, & Vassos, 2016). Furthermore, a recent case-control study conducted in different countries across Europe and Brazil found that patients presenting to psychiatric services with a first episode psychosis and controls who reported daily cannabis use had up to 3 times increased odds of psychotic disorders and up to 5 times increased odds when the type of cannabis was high-potency cannabis (Di Forti et al., 2019). The association between cannabis use and psychosis has been studied extensively, and debates continue. Nevertheless, a potential limitation of

much of the research in this area is that it has paid insufficient attention to potential variations in the potency in the types of cannabis being used.

1.6.5. Different Types of Cannabis and the Risk for Developing Psychotic-Like Experiences

Evidence has emerged that different types of cannabis might confer more risk than other types in developing psychotic-like experiences or psychotic disorders (Di Forti et al., 2015). Cannabis sativa is the plant from which different cannabis preparations are derived; the most common preparations are herbal cannabis or grass, hash and skunk or sinsemilla (Casadio et al., 2011)

Different strains of cannabis contain different concentrations of THC and CBD. Recently, a study conducted in the United Kingdom in 2018, reported the average concentrations among different cannabis samples seized from the same areas from which samples were collected in a study previously conducted in 2008 (Hardwick, 2008). Findings showed an average of 14.2% THC in cannabis type sinsemilla or skunk (Potter, Hammond, Tuffnell, Walker, & Di Forti, 2018). A study in South London, conducted amongst first episode psychosis patients, showed that individuals using skunk-like cannabis were three times more likely to have a psychotic disorder compared to those individuals that have never used cannabis. However, people using hash type cannabis did not have an increased risk compared to those who have never used cannabis, notwithstanding frequency of use (Di Forti et al., 2015).

Additionally, a study conducted in the United Kingdom, analysed hair samples of 140 individuals to examine levels of THC and CBD and identify if the presence of schizophrenia like symptoms differed, depending on THC / CBD levels found (Morgan & Curran, 2008). Three groups were identified, hair samples containing THC only, hair samples containing THC and CBD and hair samples with no cannabinoid. Researchers found that participants with only THC found in hair sample, exhibited higher levels of unusual experiences (the equivalent to positive symptoms in schizophrenia) than participants with both THC and CBD present in hair samples and those with no cannabinoids. These findings show that presence of CBD in the type of cannabis being used might decrease the risk of psychotic-like experiences induced by THC only (Morgan & Curran, 2008). Furthermore, a randomised double-blind crossover study was conducted to estimate the effects of both CBD and THC on psychotic-like experiences. Researchers found that THC increased psychotic-like experiences in laboratory-controlled conditions (Morgan et al., 2018). When examining the CBD / THC 2:1 ratio, results indicated no changes in psychotic-like symptoms in frequent cannabis users, indicating that frequent users may have a slow or weak reaction to the anti-psychotic effects of CBD.

The before mentioned studies demonstrate the importance of identifying the different types of cannabis available, potency in each type, which one is being more prevalently used and to identify the possible consequences in user's mental health according to type of cannabis. To the best of my knowledge, there is non-existent information regarding the types of cannabis being used in Mexico, and no research has been conducted previously regarding cannabis use and psychotic-like experiences. Most available research examining the association between cannabis use and psychotic-like

experiences has been conducted in either English speaking countries or European countries, therefore, the importance of conducting the present study in Mexico.

1.6.6. Conclusion

Cannabis is widely used by adolescents in Mexico City and research shows that the prevalence of use continues to increase. International research has demonstrated possible associations between cannabis use during adolescent years and an increased risk of developing psychotic-like experiences. Moreover, these associations may vary depending on the type of cannabis used, as strains with higher THC and low CBD concentrations have been found to increase the association. Although little is known about the different types of cannabis being used in Mexico, it is important to consider whether these associations vary by type of cannabis used. Moreover, it is relevant to understand the effects cannabis use is having in the adolescent population in Mexico City.

2. Cannabis Use and Psychotic Like Experiences in Adolescents: A Systematic Review

2.1. Introduction

Research has shown that cannabis use might be a risk factor in the development of psychotic disorders in adults, more specifically schizophrenia. The first study to examine the association between cannabis use and the later development of schizophrenia was conducted in an 18-year-old cohort of conscripts in Sweden. Results showed that participants reporting cannabis use on more than 50 occasions had up to six times higher risk (RR=6.0; 95CI=4.0-8.9) to be diagnosed with schizophrenia than non-users (Andreasson, 1987). Sixteen years later research in the field continued in New Zealand, where data was obtained from a multidisciplinary study of a general population birth cohort (Arseneault et al., 2002). The study examined if adolescent use of cannabis was a risk factor for the development of any type of schizophreniform disorder later in life. Results showed that participants reporting cannabis use at 15 presented more psychotic symptoms than controls (B=7.2; SE=1.07; p=0.001) after controlling for use of other drugs; furthermore, logistic regression analyses showed that participants reporting cannabis use by age 15 were up to eleven times more likely to have a diagnosis of schizophreniform disorder (OR=11.38, 95%CI=1.84-70.45; p=0.009) while controlling for use of other drugs.

A systematic review conducted to identify whether cannabis use could cause psychotic symptoms that persisted after intoxication was first conducted in 2007 (Moore et al., 2007). Results indicated an increased risk of presenting any type of psychotic-symptom in participants that reported lifetime use of cannabis (OR=1.41; 95%CI=1.20-1.65). Furthermore, higher frequency in cannabis use conferred greater risk of presenting any

psychotic-symptom (OR-2.09; 95%CI=1.54-2.84). Psychosis outcomes included any psychotic type disorder and delusion, hallucinations or thought disorder were requirements for psychotic-outcomes.

Large et al., in 2011 conducted a systematic meta-analysis to examine the extent to which cannabis use and use of other drugs impacts the age of onset of psychosis. Researchers separated cohorts by drug and examined age at onset of patients reporting substance use compared to age at onset of non-using patients. Results indicated that age of onset of psychotic illness was 2.70 (standardized mean difference=-0.414) years earlier for participants reporting specifically cannabis use than for non-users (Large, Sharma, Compton, Slade, & Nielssen, 2011).

Recently, a meta-analysis was conducted to identify if higher levels of cannabis use were significantly associated with an increased risk for psychosis (Marconi et al., 2016). Results indicate that participants using cannabis more heavily (daily, weekly, regular, 60+) were almost four times more likely to be diagnosed with schizophrenia or other psychotic-related disorders than non-users (OR=3.90; 95%CI=2.84-5.34; unadjusted).

Previous systematic reviews and meta-analyses have considered mainly the -present or absent- approach when examining the association between cannabis use and psychotic symptoms. However, research has shown that the psychotic-spectrum might be more complex and to categorise it as a dichotomous phenomenon might be a reductionist approach (Van Os, 2001). From the epidemiological perspective, psychosis could be considered as a continuum rather than as a dichotomous entity, therefore the importance of exploring experiences or symptoms rather than presence or absence of a disorder.

Systematic reviews and meta-analyses have been shown to be paramount to condense evidence regarding a specific area of interest. However, it is important to follow a methodological approach in order to cover and report all important and relevant aspects of each study (Liberati et al., 2009). To the best of my knowledge, a systematic review examining the plausible effects the use of cannabis may have in adolescents, has not been conducted until now. The present systematic review follows the PRISMA Statement methodology and examines the association between cannabis use and the occurrence of psychotic-like experiences in adolescents from the general population. Details of the methodology used are stated below.

2.2. Objectives

To conduct a systematic review of available literature to identify if adolescent cannabis use is associated with the development of psychotic-like experiences in the general population. To formulate a specific and structured research question, the PICOS (Population, Intervention, Comparison, Outcome) approach was followed.

2.3. Research Questions

- Is adolescent cannabis use associated with psychotic-like experiences in the general population?
- Is frequent and heavy adolescent cannabis use associated with psychotic-like experiences in the general population?
- Is age of onset of adolescent cannabis use associated with psychotic-like experiences in the general population?

2.4. Methods

2.4.1. Protocol and Registration

A protocol was structured in 2016 and was submitted for revision and approval for the upgrade from MPhil to PhD process in 2017.

2.4.2. Eligibility Criteria

a) Type of Participants: Participants from 9 to 26 years old, sample was restricted to general population, therefore, studies including participants with prior diagnosis of schizophrenia or another psychotic-spectrum disorder were excluded.

b) Types of Intervention: Observational studies examining cannabis use and the risk of presenting psychotic-like experiences later in life.

c) Comparator Group: Participants from 9 to 26 years old from the general population without history of cannabis use.

d) Types of Outcome Measures: Mean scores of continuous measures of psychotic-like experiences and dichotomous outcomes defined as presence or absence of psychotic-like experiences.

e) Types of Studies: Observational studies examining the risk between psychotic-like experiences and cannabis use in adolescents. Including longitudinal, retrospective, case-control and cohort studies. Restrictions regarding language were applied, and studies were only included if they were published in English or Spanish. Exclusively peered reviewed publications were included. No publication date or publication status were imposed.

2.4.3. Information Sources

Studies were identified by searching electronic databases and additional resources. Databases and resources were selected after consulting a specialist librarian at King's College London for her advice on which resource would be the most helpful to identify studies to include in the present study. The main electronic databases searched included: Applied Social Sciences Index and Abstracts (ASSIA), Cumulative Index to Nursing and Allied Health Literature (CINHAL), Cochrane Library, Excerpta Medica Database (EMBASE), Health Management Information Consortium (HMIC), International Pharmaceutical Abstracts (IPA), MEDLINE, PsycINFO, PubMed, Scopus and Web of Science.

2.4.4. Search

Search strategies were developed by exploring each database's subject headings and MESH terms related to the main interest of the review ('cannabis' + 'adolescence' + 'psychotic-like experiences' including synonyms); every database had a unique search strategy as search terms for each one was different. Once all the search strategies were structured and reviewed, searches were run, the results were saved and exported to EndNote for screening. The search strategy conducted for EMBASE is presented below and unique strategies for each database can be found in the Appendix.

2.4.5. Search Strategy

1. Substance abuse

   Drug abuse

2. Cannabis

   Cannabis addiction

Cannabis-induced psychosis

Cannabis smoking

3. Marijuana
4. Cannabis use

   Tetrahydrocannabinol
5. Adolescent
6. Psychotic symptom* / Psychotic ADJ5 Symptom*
7. Psychosis

   Cannabis-induced psychosis
8. Prodrom* symptom* / Prodrom* ADJ5 Symptom*
9. Vulnerability for psychosis / Vulnerability ADJ5 Psychosis

   Disease predisposition
10. Early onset psychosis / Early ADJ5 Psychosis
11. First episode psychosis / First ADJ5 Psychosis
12. Psychotic like experiences / Psychotic ADJ5 Experiences

((“substance abuse”) OR (“substance related disorders”) OR (cannabis) OR (marijuana) OR (“cannabis use”) OR (“marijuana abuse”) OR (“marijuana smoking”)) AND ((adolescent) OR (“adolescent psychiatry”)) AND ((“psychotic symptom*”) OR (psychotic adj5 symptom*) OR (psychosis) OR (“prodrom* symptom*”) OR (prodrom* adj5 symptom*) OR (“vulnerability for psychosis”) OR (vulnerability adj5 psychosis) OR (“substance-induced psychoses”) OR (“early onset psychosis”) OR (early adj5 psychosis) OR (“first episode psychosis”) OR (first adj5 psychosis) OR (“psychotic like experiences”) OR (psychotic adj5 experiences))

2.4.6. Study Selection

Eligibility assessment for the inclusion of studies was conducted individually by two different reviewers. Once the screening process was completed, disagreements were resolved after discussion and consensus by both reviewers.

2.4.7. Data Collection Process

A data extraction sheet was developed in line with the Cochrane Consumers and Communications Review Group's data extraction template, modified for the specific aims of the present review. Data extraction was conducted by one author.

2.4.8. Data Items

The following data were extracted from each individual study: authors, country were the study was conducted, study design, number of participants included in analyses, cannabis use assessment, psychotic-like experiences assessment, prevalence of cannabis use, prevalence of psychotic-like experiences, covariates, types of analyses, estimated effect size, odds ratios and/or unstandardized beta depending on the type of analysis conducted.

2.4.9. Risk of Bias within Individual Studies

The Newcastle-Ottawa Scale was employed for assessing the quality of individual studies. It helps with the assessment of non-randomized study designs by evaluating selection of the study group, comparability of study groups, and the ascertainment of the outcome (Wells, 2014). Results are shown in Table 2.4, Table 2.5 and Table 2.6.

2.4.10. Summary Measures

Depending of the type of analysis conducted in each study data were identified accordingly. For logistic regression analyses, odds ratios of both adjusted and unadjusted models alongside their respective confidence intervals were extracted and for linear regression analysis unstandardized beta, standard deviation and p-values.

2.4.11. Synthesis of Results

Studies included varied in the type of analyses conducted. Two main type of analyses were identified, linear regression analyses and logistic regression analyses. Twelve of the included studies analysed their data using linear regression, sixteen employed logistic regression and, of those studies, four were included in both groups as they conducted both type of analyses. Three studies included in the systematic review were not included in either group as the type of analysis employed differed from the before mentioned analyses. Data can be observed in Table 2.3.

2.4.12. Risk of Bias across Studies

No risk of bias assessment across studies was conducted.

2.4.13. Additional Analyses

No additional analyses were conducted.

2.5. Results

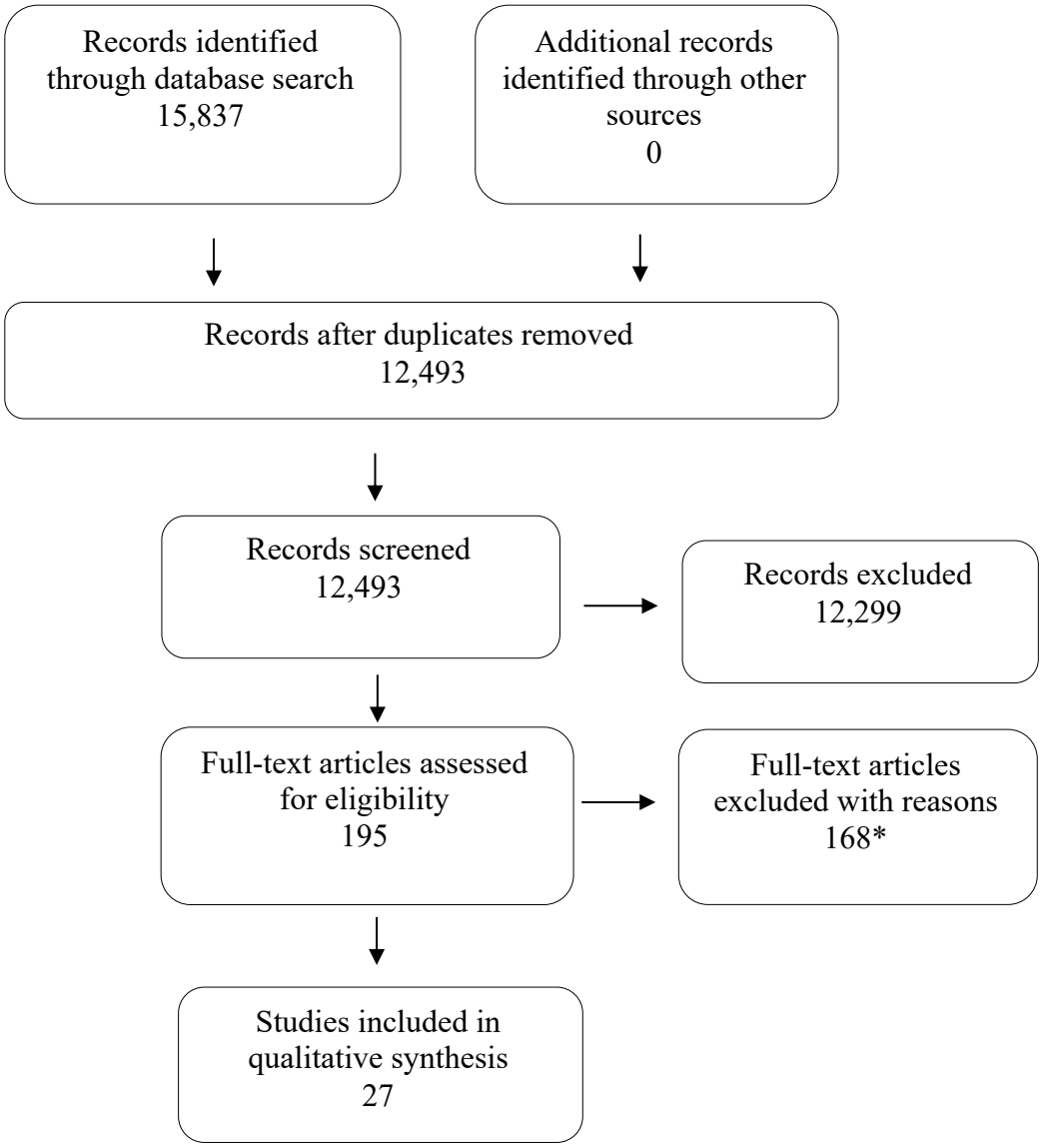
2.5.1. Study Selection

A final search was conducted on the 3rd of July 2019. No date limit was imposed, therefore all available papers in the databases searched were included in the screening process. Searches were conducted in eleven electronic databases which provided 15,837 references. After duplicate removal, from the eleven databases, 12,493 references were screened by title and/or abstract and 195 of these were selected for full-text screening. A total of 168 references were excluded and 27 were included in the systematic review as they met the inclusion criteria.

2.5.2. Reasons for Exclusion

After full text screening was conducted on the 195 eligible studies, 168 papers were excluded. Reasons for exclusion are the following: study identified was a review, letter to editor, opinion article, systematic review, meta-analysis or conference abstract; participants did not meet the inclusion criteria, there was no age range provided, predictor or outcome variable was not of interest for the present review and publication was not in English or Spanish language.

Figure 2.1 PRISMA Flow Diagram



2.5.3. Study Characteristics

Twenty-seven papers were found that met the inclusion criteria. Of the 27 studies included in the systematic review, nineteen had a longitudinal design, nine cross-sectional and one identified as retrospective. Overall, the included studies comprised 75,081 participants, with an age range of 9 to 26 years old. Sixteen studies ran logistic regression analyses to identify risk. Eight conducted linear regression analysis to examine associations between cannabis use and psychotic-like experiences. Three studies conducted different analyses to the ones mentioned above. One conducted Cox Regression Analysis Survival Time and Hazard Ratios, the second study conducted Spearman Correlation Test, Multivariate Econometric Linear Regression Model and Mann-Whitney U Test and, lastly, the third study conducted Multivariate Analysis of Variance (MANOVA), Chi-Square Analysis, Partial eta Squared for Effect Size, Mediation Analysis and Sobel Test to verify the significance of the possible indirect effect.

Studies were conducted in New Zealand (2), Germany (2), Finland (2), Netherlands (3), Switzerland, United Kingdom (3), United States of America (4), Canada, Denmark, Greece, Australia (2), Trinidad y Tobago, Brussels and Spain. The first study included in the present review was published in 2002 and the last one was conducted in 2019. Specific data regarding types of assessment by individual studies can be observed in Table 2.1, Table 2.2 and Table 2.3. Three tables were structured according to type of analysis in order to facilitate structure.

2.5.4. Results of Individual Studies

Table 2.1 Study Characteristics: Logistic Regression Analyses

#	Author, Year & Country	Study Design & Participants	Assessments	
			Cannabis Use	**Psychotic-Like Experiences**
1*	Arseneault, L. et al. (2002) New Zealand	Prospective Longitudinal Cohort 759	Controls Never or once: Cannabis users at age 15: three times or more Cannabis users at age 18: three times or more	Standardized interview scheduled (DSM-IV)
2*	Fergusson, D.M. et al. (2003) New Zealand	Longitudinal 1,053	Composite International Diagnostic Interview (CIDI) Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)	Items from the Symptom Checklist 90 (SCL-90)
3	Henquet, C. et al. (2005) Germany	Prospective Cohort 2,437	Munich-Composite International Diagnostic Interview (M-CIDI)	(M-CIDI) (SCL-90)
4	Miettunen, J. et al. (2008) Finland	Prospective Cohort 6,330	Self-completion questionnaire	PROD-Screen
5	Kuepper, R. et al. (2011) Germany	Prospective Cohort 1,930	Munich-Composite International Diagnostic Interview (DIA-X/M-CIDI)	(DIA-X/M-CIDI)
6	Schubart, C. et al. (2011) Netherlands	Cross-sectional 17,698	Euros spent on cannabis	Community Assessment of Psychic Experiences (CAPE)
7	Roessler, W. et al. (2011) Switzerland	Longitudinal 4,547	Structured Psychopathological Interview and Rating of the Social Consequences of Psychological Disturbances for Epidemiology (SPIKE)	"Schizotypal Signs" "Schizophrenia Nuclear Symptoms"
8	Mackie, C. et al. (2013) UK	Prospective Longitudinal 1,098	Reckless Behaviour Questionnaire	Diagnostic Interview Schedule
9	Gage, S. et al. (2014) UK	Cohort Study 1,756	Self-report questionnaire	Semi-structured interview (PLIKSi: Zammit et al. 2013)
10*	Bechtold, J. et al. (2016) USA	Longitudinal 1,009	Youth-reported substance use questionnaire	Youth Self Report: Subclinical psychotic symptoms
11*	Bourque, J. et al. (2017) Canada	Prospective Longitudinal 3,096	Detection of Alcohol and Drug Problems in Adolescence	Adolescent Psychotic Symptom Screener

#	Author, Year & Country	Study Design & Participants	Assessments	
			Cannabis Use	Psychotic-Like Experiences
12	Jones, J., et al. (2017) USA	Cross-sectional 4,208	Abbreviated and locally computerized version of the Minnesota Centre for Twin and Family Research self-report substance use measure	GOASSSESS, a computerized, structured interview adapted from the Kiddie Schedule for Affective Disorders and Schizophrenia
13	Shevlin, M. et al. (2017) Denmark	Retrospective Birth Cohort 2,980	"Have you ever tried…"	ICD-10
14	Jones, H., et al. (2018) England	Longitudinal Cohort Study 5,300	No use of cannabis or cigarettes Cigarette only Cannabis with or without	Semi-structured psychosis-like symptom interview (PLIKSi)
15	Mustonen, A., et al. (2018) Finland	Birth Cohort Longitudinal 6,534	Lifetime use and frequency of use (never, once, 2-4 times, 5 times or more or regularly	Psychosis Diagnosis: ICD-10 Prodromal Symptoms: PROD-Screen
16	Levy, S. et al. (2019) USA	Cross-sectional 527	Standardized questions about symptoms of cannabis use disorder based on the modified World Mental Health Composite International Diagnostic Interview	"In the past 12 months, how often have you felt anxious or paranoid during or after using marijuana?" "In the past 12 months, how often have you seen, felt, or heard things that were not really there (i.e., hallucinations) during or after using marijuana?"

Table 2.2 Study Characteristics: Linear Regression Analyses

#	Author, Year & Country	Study Design & Participants	Assessments	
			Cannabis Use	Psychotic-Like Experiences
1*	Arseneault, L. et al. (2002) New Zealand	Prospective Longitudinal Cohort 759	Controls: Never or once Cannabis users at age 15: three times or more Cannabis users at age 18: three times or more	Standardized interview scheduled (DSM-IV)
2*	Fergusson et al. (2003) New Zealand	Longitudinal 1,053	(CIDI) (DSM-IV)	(SCL-90)
3	Stefanis, N. et al. (2004) Greece	Cross-Sectional 3,500	Cannabis lifetime frequency use (never, once, 2-4 times, 5 times or more) Systematic Use: Daily or Almost Daily	Community Assessment of Psychic Experiences (CAPE)
4	Hides, L. et al. (2009) Australia	Cross-Sectional 880	Youth Risk Behaviour Survey (YRBS)	Community Assessment of Psychiatric Experiences (CAPE)

#	Author, Year & Country	Study Design & Participants	Assessments	
			Cannabis Use	Psychotic-Like Experiences
5	Konings, M. et al. (2008) Trinidad y Tobago	Cross-Sectional 472	Questionnaire on past and current cannabis use	Community Assessment of Psychic Experiences
6	Anglin, D. et al. (2012) USA	Longitudinal 804	Non-users: Experimented once or twice Users: At least monthly use Early CU: before 14 years old	Children in the Community Self Report Schizotypal Personality Disorder Scale
7	Van Gastel, W. et al. (2011) Netherlands	Observational Cross-sectional 4,552	Frequency of cannabis use (never, ever but not past year, once or twice during past year, between 3 and 39 times)	Community Assessment of Psychic Experiences (CAPE)
8	Griffith-Lendering, M. et al. (2012) Netherlands	Longitudinal 2,230	Self-report items regarding frequency in the last year	Youth Self-report subscales
9*	Bechtold, J. et al. (2016) USA	Longitudinal 1,009	Youth-reported substance use questionnaire	Youth Self Report: Subclinical psychotic symptoms
10*	Bourque, J. et al. (2016)	Prospective Longitudinal 3,069	Detection of Alcohol and Drug Problems in Adolescence	Adolescent Psychotic Symptom Screener
11	Albertella, L. et al. (2018) Australia	Longitudinal 155	Lifetime use Past 6 months use Frequency of use past six months Frequency of use past month	Adapted version of the short form of the Oxford-Liverpool Inventory of Feeling and Experiences
12	Leadbeater, B. et al. (2018) Canada USA	Longitudinal 662	Past year use (0= never to 4=more than once a week) Mini-International Neuropsychiatric Interview	Symptoms Checklist 90-Revised (SLC-90)

Table 2.3 Study Characteristics: Other Analyses

#	Author, Year & Country	Study Design & Participants	Assessments	
			Cannabis Use	**Psychotic-Like Experiences**
1	Ferdinand, R. et al. (2005) Netherlands	Longitudinal Cohort Study 2,076	Composite International Diagnostic Interview (CIDI)	Composite International Diagnostic Interview (CIDI) Lifetime symptoms
2	Bernardini, F. et al. (2018) Brussels	Cross-Sectional 257	Lifetime and current cannabis use	Aberrant Salience Inventory (ASI) Assessment of Psychic Experiences (CAPE)
3	Fonseca-Pedrero, E. et al. (2019) Spain	Cross-sectional 1,588	Modified Substance Use Questionnaire (Abbreviated Assist)	Prodromal Questionnaire-Brief (PB-Q)

2.5.5. Risk of Bias within Studies

Risk of bias within studies was assessed using the Newcastle-Ottawa Scale. The aim of the scale is to assess the quality of non-randomized studies to be used in systematic reviews (Wells, 2014). The maximum score a study can have is nine, indicating that the quality of said study is high. The pointing rate score depends on selection process, comparability and outcome. The selection process assesses the selection of the cohorts, ascertainment of exposure and demonstration that outcome of interest was not present at the start of the study. Comparability assesses that both cohorts are matched and that confounders are or not adjusted in the analyses and, lastly, outcome assesses how exposure is measured if acquired.

Four studies in the present review score nine (Fergusson et al., 2003; Henquet et al., 2005; Kuepper et al., 2011; Mackie et al., 2013), six scored eight (Anglin et al., 2012; Arseneault et al., 2002; Gage et al., 2014; Jones et al., 2018; Mustonen, Niemela, et al., 2018; Roessler, Hengartner, Angst, & Ajdacic-Gross, 2012), three scored seven (Bourque, O'Leary-Barrett, & Conrod, 2016; Ferdinand et al., 2005; Griffith-Lendering et al., 2013), four scored a total of six (Albertella, Le Pelley, Yucel, & Copeland, 2018; Miettunen et al., 2008; Shevlin et al., 2017; Stefanis et al., 2004), four scored five (Jones, Calkins, Scott, Bach, & Gur, 2017; Leadbeater, Ames, & Linden-Carmichael, 2019; Levy & Weitzman, 2019; Schubart et al., 2011), five scored four (Bechtold et al., 2016; Bernardini et al., 2018; Fonseca-Pedrero et al., 2019; Hides, Lubman, Cosgrave, Baker, & Yung, 2008; Konings, 2009) and only one three (van Gastel et al., 2012).

Table 2.4 Risk of Bias within Studies: Logistic Regression

Study	Selection (Max. 4)	Comparability (Max. 2)	Outcome (Max. 3)	Total (Max. 9)
Arseneault et al., 2002	3	2	3	8
Fergusson et al., 2003	4	2	3	9
Henquet et al., 2005	4	2	3	9
Miettunen et al., 2008	3	2	1	6
Kuepper et al., 2011	4	2	3	9
Schubart et al., 2011	3	2	0	5
Roessler et al., 2012	3	2	3	8
Mackie et al., 2013	4	2	3	9
Gage et al., 2014	3	2	3	8
Bechtold et al., 2016	1	1	2	4
Bourque et al., 2016	3	2	2	7
Jones et al., 2017	2	2	1	5
Shevlin et al., 2017	3	2	1	6
Jones et al., 2018	4	1	3	8
Mustonen et al., 2018	3	2	3	8
Levy et al., 2019	3	1	1	5

Table 2.5 Risk of Bias within Studies: Linear Regression

Study	Selection (Max. 4)	Comparability (Max. 2)	Outcome (Max. 3)	Total (Max. 9)
Stefanis et al., 2004	2	2	2	6
Hides et al., 2009	2	2	0	4
Konings et al., 2009	2	2	0	4
Anglin et al., 2012	4	2	2	8
Van Gastel et al., 2012	2	1	0	3
Griffith-Lendering et al., 2013	3	2	2	7
Albertella et al., 2018	3	2	1	6
Leadbeater et al., 2018	2	1	2	5

Table 2.6 Risk of Bias within Studies: Other Analyses

Study	Selection (Max. 4)	Comparability (Max. 2)	Outcome (Max. 3)	Total (Max. 9)
Ferdinand, et al., 2005	4	1	2	7
Bernardini et al., 2014	3	1	0	4
Fonseca-Pedrero et al., 2019	3	1	0	4

2.5.6. Synthesis of Results

2.5.6.1. Cannabis Use and Psychotic-Like Experiences in Adolescents

In the present systematic review, results showed that cannabis use during adolescence may increase the risk for experiencing psychotic-like experiences in the general population. Five studies, mainly examining the association of any adolescent cannabis use and psychotic-like experiences showed that even after adjustment for different confounders, cannabis use continued to be a significant risk factor for experiencing psychotic-like experiences (Henquet et al., 2005; Kuepper et al., 2011; Miettunen et al., 2008; Roessler et al., 2012; Stefanis et al., 2004).

Henquet et al., in 2005 found that cannabis use at baseline increased the incidence of psychotic-like experiences at follow-up, four years later. This finding remained significant while adjusting for age, gender, socioeconomic status, urbanicity, childhood trauma, predisposition for psychotic-like experiences and use of other drugs including tobacco and alcohol (OR=1.53, 95% CI=1.13-2.07). Overall, results showed that cannabis use increases the risk of psychotic-like experiences in young people, however, the effect appeared stronger in adolescents with predisposition for psychosis.

In line with these results, other studies continued to find that use of cannabis in adolescence increased the likelihood of appearance and persistence of psychotic-like experiences independent of age, gender, socioeconomic status, use of other drugs, urban or rural environment, childhood trauma and comorbidity (Miettunen et al., 2008; Roessler et al., 2012; Stefanis et al., 2004).

Furthermore, one study that specifically examined to what extent the associations between cannabis use, cigarette use and psychotic-like experiences can be explained by confounding found that, after adjustment of pre-birth and childhood confounders, and after excluding experiences credited to cannabis intoxication, the association remained significant. There was a 48% increase (95%CI=1.18-1.86) in risk across different categories of psychotic-like experiences at age 18 for every unit of increase in cannabis use at age 16 (Gage et al., 2014). However, it is worth mentioning that when adjustment for use of other drugs was made, the association did not remain significant (OR=1.09, 95%CI=0.65-1.82) between cumulative cannabis use at 16 years old and psychotic-like experiences at 18 while excluding psychotic-like experiences at age 12 and 16 years old (Gage et al., 2014).

Table 2.7 Cannabis Use and Psychotic-Like Experiences in Adolescents

Author & Year	Adjusted		95%	p	Covariates
	B	OR			
Henquet, 2005	-	1.53	1.13-2.07	-	Age, gender, SES, other drug use, depressive, symptoms, urbanicity, childhood trauma, predisposition for psychosis
Miettunen, 2008	-	2.23	1.70-2.94	-	Gender, family type, early emotional and behavioural symptoms, SES, tobacco use, other drug use, parental substance use disorder
Kuepper, 2011	-	1.9	1.1-3.1	-	Age, gender, SES, use of other drugs, childhood trauma, urbanicity, pre-existing psychotic symptoms
Stefanis, 2004*	0.96	-	-	0.000	Gender, school grade obtained, other drug use, CAPE dimensions
Gage, 2014	-	1.09	0.65-1.82	-	Pre-birth and childhood confounders, alcohol and cigarette use, use of other drugs and after excluding PLE's at 12 and 16
Shevlin, 2017	-	5.96	1.71-20.75	-	Gender, parental psychosis and use of other drugs

Author & Year	λ, F		p	Covariates
Fonseca-Pedrero, 2019	-	λ=0.994 F=5.05	-	0.007	Age, gender, SES, smoking, alcohol use, IQ, emotional behavioural problems

***** *Multiple measures paranoia and systematic use.*

On the other hand, Shelvin et al. in 2017, found that when separating participants by cannabis use only from cannabis use + use of other drugs, the use of cannabis alone was not significantly associated with psychotic-like experiences. However, cannabis use + use of other drugs showed a statistically significant association with the appearance of psychotic-like experiences. Initially, the bivariate association between cannabis use and psychotic-like experiences was significant. Nevertheless, when adjusting for gender and parental history of psychosis, logistic regression analyses showed that the association was no longer significant (Shevlin et al., 2017).

Similarly, another study found that the link between cannabis use and psychotic-like experiences disappeared when adjusting for gender, age, socioeconomic status, use of tobacco and alcohol, behavioural and emotional problems and intelligence quotient (Fonseca-Pedrero et al., 2019). Researchers examined if emotional and behavioural problems may mediate the before mentioned association and it was found that cannabis use, firstly increased the risk for other types of psychopathology and, in result, the appearance of psychotic-like experiences (Fonseca-Pedrero et al., 2019).

2.5.6.2. Early Onset of Cannabis Use

Nine studies included in the systematic review, in addition to examining the association between cannabis use and psychotic-like experiences, examined if early onset of cannabis use had a stronger effect on the appearance of psychotic-like experiences (Albertella et al., 2018; Anglin et al., 2012; Arseneault et al., 2002; Jones et al., 2018; Konings, 2009; Mackie et al., 2013; Schubart et al., 2011; Stefanis et al., 2004; van Gastel et al., 2012).

Studies showed that using cannabis earlier in adolescence increased the risk of developing psychotic-like experiences later in life, and the association remained after adjusting for confounding factors. Confounder factors taken into account included in the analyses were the following; psychotic symptoms, use of other drugs (Arseneault et al., 2002); other drug use, other dimensions of CAPE, gender, school grade, lifetime experience of distress associated with positive psychotic experiences (Stefanis et al., 2004); age, school type, ethnicity, gender, current use of cannabis, use of other drugs (Konings, 2009); age, gender, level of education (Schubart et al., 2011); adolescent schizotypal symptoms, major depression, anxiety disorders, cigarette use, other drug use (Anglin et al., 2012); age, gender, household composition, family affluence, social support, alcohol use, daily smoking, ethnicity and urbanization (van Gastel et al., 2012); demographics, depression, cigarette, alcohol and other drug use and previous psychotic-like experiences (Mackie et al., 2013).

Furthermore, in a more recent study, cannabis use remained significantly associated with psychotic-like experiences after controlling for a significant number of confounding factors gender, family history of depression, schizophrenia, other drug use, maternal or parental smoking during pregnancy, maternal education, highest parental social class, IQ, childhood trauma or bullying, emotional and behavioural problems and alcohol use, cigarette use (Jones et al., 2018). Early cannabis use was classified as such if onset was prior age 12 to 16, depending on the study. However, there have been some exceptions where researchers have not found that earlier onset of cannabis use confers a greater risk for psychotic-like experiences than later onset of cannabis use. Two studies that examined the association between age of onset of use and risk of psychotic-like

experiences did not find any indicator that early onset had a stronger association than later onset of use (Jones et al., 2017; Leadbeater et al., 2019).

Table 2.8 Early vs. Late Onset of Cannabis Onset and Psychotic-Like Experiences

Authors & Year	Early Cannabis Use				Late Cannabis Use	
	OR	95%CI	B	p	OR	95%CI
Arseneault, 2002	11.38	.84- 70.45	-	-	1.95	0.76, 5.01
Stefanis, 2004*	-	-	0.74	0.001	-0.18	0.25
Konnings, 2008	-	0.22-1.19	0.71	-	-0.11	-0.57-0.36
Schubart, 2011	1.82	1.23-2.70	-	-	1.18	0.90-1.55
Anglin, 2012§	-	-	.18	.05	NR	NR
Van Gastel, 2011	-	-	0.081	0.000	NR	NR
Mackie, 2013∞	2.54	1.22-5.23	-	-	1.66	0.67-4.15
Albertella, 2018	-	-	0.31	0.001	NR	NR
Jones, 2018	3.70	1.66-8.25	-	-	2.97	1.63, 5.40

**Only reported measure for the hallucinations scale, for data on all scales see the Appendix, adjusted for frequency of use and all scales remained significant after controlling for frequency of use. §For data on all models see the Appendix. ∞Trajectory class comparison of PLE's: Elevated vs. Low.*

2.5.6.3. Frequent, Heavy and Cumulative Cannabis Use and Psychotic-Like Experiences

When conducting research in cannabis use and psychotic-like experiences, one important component in the link that has been found, is that frequent use, heavy use and cumulative history of use may play an important role in the association. From the included studies in the present review, five found a dose response relationship;

indicating that the risk of presenting psychotic-like experiences increased linearly with the increment of cannabis use (Bourque et al., 2016; Henquet et al., 2005; Miettunen, Niemelä, & Mustonen, 2018; Miettunen et al., 2008; van Gastel et al., 2012).

Moreover, six studies found that frequent cannabis use had a significant effect on the appearance of psychotic-like experiences and, regular cannabis use predicted higher levels of psychotic-like experiences (Anglin et al., 2012; Bourque et al., 2016; Hides et al., 2008; Levy & Weitzman, 2019; Mustonen, Niemela, et al., 2018; Roessler et al., 2012). Similarly, heavy cannabis use, including cannabis use disorders, were equally linked to an increased risk of presenting the before mentioned experiences compared to non-users or non-heavy, non-dependent cannabis users (Fergusson et al., 2003; Levy & Weitzman, 2019; Schubart et al., 2011; van Gastel et al., 2012). Research has shown that cannabis use may have a cumulative and sustained effect, and that regular cannabis use increases the risk in the appearance of psychotic-like experiences which may persist over time; despite discontinuing its use (Bechtold et al., 2016; Bourque et al., 2016).

Table 2.9 Frequent, Heavy and Cumulative vs. Non-Frequent, Non-Heavy and Non-Cumulative Cannabis Use

Authors & Year	Frequent, Heavy or Cumulative			Non-Frequent, Heavy or Cumulative	
	OR	**95%CI**	**p**	**OR**	**95%CI**
Henquet, 2005	2.23	1.30-3.84	-	1.53	1.13-2.07
Miettunen, 2008	1.42	1.23-1.64	-	NR	NR
Schubart, 2011	3.54	2.94-4.26	-	0.96	0.82-1.13
Roessler, 2012	2.29	1.32-3.97	-	1.80	1.22-2.66
van Gastel, 2011	0.065	-	0.000	0.037	0.018
Bourque, 2016	2.59	1.11-6.03	-	NA	NA
Bechtold, 2016	1.51	1.08-2.11	-	1.15	0.91-1.46
Levy et al., 2019	3.81	1.71-8.50	-	NR	NR
Mustonen, 2018	**HR** 3.02	1.14-7.98	-	1.15	0.46-2.95
Fergusson, 2003	**RR** 1.8	1.2-2.6	-	NA	NA
Hides, 2009	**M** 29.4 **SD** 5.7	-	<0.05	31.2	NR
Leadbeater, 2019	**B** 0.13	0.002-0.25	-	NR	NR

**HR= Hazard Ratio; RR= Risk Ratio; M=Mean; SD=Standard Deviation; B=Beta*

2.5.6.4. Bi-Directional Relationship between Cannabis Use and Psychotic-Like Experiences

Lastly, two studies included in the present review found a bi-directional relationship between these variables; Ferdinand, in 2005 and Griffith-Lendering in 2012 found that cannabis use predicted psychotic-like experiences and that presence of these experiences also predicted subsequent cannabis use (Ferdinand et al., 2005; Griffith-Lendering et al., 2013). Nevertheless, other studies did not find such bi-directionality,

showing that it was only cannabis use that predicted psychotic-like experiences later in life (Bechtold et al., 2016; Kuepper et al., 2011).

2.6. Discussion and Conclusion

2.6.1. Summary of Evidence

This systematic review identified 27 studies that have examined the association between cannabis use and psychotic-like experiences in adolescents. Overall, most studies demonstrated that cannabis use in adolescence may increase the risk of presenting psychotic-like experiences later in life. Risk remained significant after adjusting for confounding factors. However, these findings were not consistent across all studies, results of two different studies indicated the opposite; once researchers adjusted for confounding factors the association disappeared.

One consistent finding across all studies which examined frequent, heavy and cumulative use of cannabis was that there is a dose-response effect on the association between cannabis use and psychotic-like experiences. That is that the more frequent, the more quantity and the longer participants used cannabis, the higher the risk and the strength of the relationship with the development of psychotic-like experiences.

Furthermore, some of the included studies, demonstrated that age of onset of cannabis use may have an increased impact in the association, indicating that earlier onset of cannabis use significantly increased the risk of presenting psychotic-like experiences. However, similarly to the findings regarding control for confounding factors, results of two studies did not find this increased risk, reporting that early onset of cannabis use was not significantly associated with psychotic-like experiences.

Lastly, the bi-directional relationship of cannabis use and psychotic-like experiences had also mixed findings. Whereas two studies did find this relationship, two other studies showed that cannabis use did predict psychotic-like experiences, however, psychotic-like experiences did not predict cannabis use later in life, indicating inconsistent results across said hypotheses.

Twenty-seven of the twenty-nine included studies confirmed that cannabis use during adolescence is significantly associated with presence of psychotic-like experiences later in life. In spite of some studies not finding a significant association after controlling for confounding factors, most studies did, and these results should be considered and taken into account for the development of public policies and the information provided to the general population regarding cannabis use. A number of different factors may influence and shape the relationship between cannabis use and psychotic-like experiences, and unfortunately, not all studies took all factors into account. Some of the factors that have been shown to influence the appearance of said experiences are childhood trauma, family history of psychotic-spectrum disorders, use of other drugs, urbanicity, etc. Furthermore, research has shown that genetic vulnerability may play an important role in the development of psychotic-experiences or episodes when using cannabis (Løberg et al., 2014), which indicates that there are more than only environmental factors that may be interacting in the association between cannabis use and psychotic-like experiences.

2.7. Limitations of Studies Included

One of the main difficulties while conducting this systematic review was choosing the included studies, as the outcome of psychotic-like experiences or psychosis was

extremely heterogeneous. The assessments employed by each study were different and this made the process very complex. Furthermore, as each study adjusted for different confounds, this made analysing the data markedly difficult.

Moreover, one limitation across studies is that there was no assessment of type of cannabis used. This is important to consider when examining the association between cannabis use and psychotic-like experiences as different studies have shown that high-potency cannabis tend to increase risk for psychosis (Di Forti et al., 2009). Furthermore, some studies did not assess use of illicit drugs, which research has shown to be significantly associated with psychotic-like experiences and, when included in adjusted models, attenuates the association between cannabis use and psychotic-like experiences significantly.

2.8. Strengths and Limitations

To the best of my knowledge, this is the first systematic review examining cannabis use and psychotic-like experiences in an adolescent population. There have been previous systematics reviews conducted which examined cannabis use and psychosis, nevertheless the target populations were different (Large et al., 2011; Marconi et al., 2016; Moore et al., 2007; Myles, Myles, & Large, 2016; Schoeler et al., 2016).

Furthermore, eleven databases were searched, and this resulted in a substantial number of resources. A limitation to be considered is that only one author conducted the screening process and was responsible of extracting data from the included studies. The process was conducted at two separate times points in a very thorough and comprehensive manner.

3. Methodology

3.1. Overview of Study Design

This is a cross-sectional study designed to examine the relationship between cannabis use and psychotic-like experiences in adolescents in Mexico City and Estado de Mexico. Data were collected from two adolescent samples: a general population sample recruited from state funded middle schools and a clinical sample of adolescents experiencing cannabis related problems recruited from drug use treatment services. Participants in both samples completed questionnaires describing a) sociodemographic characteristics; b) patterns of cannabis use; c) cannabis use after-effects; d) psychotic-like experiences; e) potentially confounding variables including use of other drugs. A detailed description of the procedures used in this study is provided below.

3.2. Adolescent Student Sample

The school sample was recruited from seven different public middle schools located in four different boroughs in Mexico City and the surrounding county, Estado de Mexico; Iztapalapa, Tlanepantla, Gustavo A. Madero and Ecatepec. An in-depth description of the school system in Mexico is provided below as well as a detailed description of the boroughs from where data were collected. This description aims to help as background of how the school system works in Mexico, school attendance by age and borough, the sociodemographic characteristics of the boroughs from where data was collected and from the drug services attended.

3.2.1. School System in Mexico

Mexico has a total population of 119,938,473 of which 48.6% are men and 51.4% are women (INEGI, 2015). Part of the target age range of this study, 16 to 19 year olds,

comprise 9% of the total population in Mexico (INEGI, 2015). Mexico City has a total population of 8,918,653 which comprises 7.5% of the total population in Mexico; Estado de México is populated by 17,604,619 people which comprises 13.5% of Mexico's total population being the most populated county in the country and it is characterised by its location, surrounding most parts of Mexico City (INEGI, 2017a).

The percentage of 15 to 24-year olds in 2015 that reported attendance to some type of education centre was 44% (INEGI, 2015). The national school system in Mexico is structured of 3 different levels; a) basic education, b) middle education and c) higher education; which are also divided into public and private sectors, with 86% of pupils attending public schools at a national level and 14% to private schools (SEP, 2018). Basic education encompasses preschool, primary school and secondary school, which are all compulsory. Middle school includes A Levels, all levels equivalent to this and professional education that does not require A Levels or its equivalents. Compulsory ages for school attendance in Mexico are from 3 to 16 years old, the first level, preschool from the age of 3 to 5 years old. Next, primary school is structured by 6 grades, where the age range is from 6 to 12 years old. Lastly, secondary school with 3 grade levels, where age ranges from 12 to 16 years old. Middle school and graduate school are not compulsory. In order to provide a comparison of the school population with the general adolescent population in Mexico, school attendance data is provided below. Furthermore, specific school attendance data regarding each of the boroughs from where data was collected in the present study is included (SEP, 2018).

In Mexico there are two different methods to obtain middle school education: on campus and by distance learning. On campus means that students are required to attend

school from Monday to Friday, full time during the duration of the school year; distance learning allows students to either only attend school part time or not to attend at all and only present exams to pass each subject, once all subjects have been completed, students can graduate from middle school. The most common method, however, is on campus with 92% of middle school students enrolled whereas only 8% are enrolled in distance learning (SEP, 2018). From the 92% of students enrolled on campus, 80% were in public schools and 20% reported attending private on campus middle schools. The drop-out prevalence in middle school throughout Mexico is of 13.3% (SEP, 2018).

Specifically, in Mexico City there where 476,825 pupils enrolled in middle school in the school year 2017-2018. In total in the city there are 249 public middle schools and 403 private schools. Sixty-five percent of students in the city in middle school were enrolled on campus from which 72% were in public schools and 28% in private schools. Thirty-five percent were on the distance learning method from which 99% reported being in a public school and only 1% in private distance learning method. In Mexico City the total dropout rate of middle school students aged 15 to 19-year olds approximately, is 17.9% including both, on campus and distance learning (SEP, 2018).

School attendance in Mexico by age in 2017 was reported as follows; 85% of 14-year olds reported attending school, 75% of 15-year olds, 72% of 16-year olds and 70% of 17-year olds. From the age of 18 school attendance in the country decreases significantly with only 45% of 18-year olds and only 37% of 19-year olds reporting school attendance. When examining specifically school attendance in Mexico City, in 2017 it was reported that 95% to 82% of 14 to 16-year olds were attending school, whereas only 78% to 56% of 17 to 19-year olds were attending school. In contrast, in

Edo. de Mexico, numbers were significantly different, with 93% to 76% of 14 to 16-year olds and 70% to 44% of 17 to 19-year olds were attending to school this same year (INEGI, 2017b).

However, when observing the specific boroughs from where data was collected it was observed that rates of school attendance by age were lower than the average of the city's mean rates. In Gustavo A. Madero 93% to 78% of 14 to 16-year olds and 72% to 53% of 17 to 19-year olds reported school attendance. In Iztapalapa 92% to 73% of 14 to 16-year olds and only 66% to 45% of 17 to 19-year olds reported school attendance (significantly lower than the city average). In Estado de Mexico, in both counties, Ecatepec and Tlanepantla only 55% of 15 to 17-year olds reported school attendance (SEP, 2018).

3.2.2. Adolescent Student Sample: Recruitment and Sampling

Schools were contacted and invited to participate in the study via Juvenile Inclusion Centres with the support of the workforce from each treatment centre. A detailed description of what Juvenile Inclusion Centres are and its role and involvement in the study is provided below.

3.2.3. Adolescent Student Sample and Juvenile Inclusion Centres

Juvenile Inclusion Centres (CIJ) is a non-profit organisation created in Mexico in 1969 which provides prevention and treatment services for addiction related problems. Its main objective is to contribute in the reduction of drug use within the community, through their participation in prevention and treatment. Its national workforce is formed of 117 units across Mexico; eleven are inpatient centres and 2 of them are specifically

targeted to heroin users located in high risk areas; the remaining units are outpatient treatment services which also provide prevention workshops in schools and within the community. These centres are funded by the government and by private contributions (Juvenile Inclusion Centres, 2018).

As previously mentioned, part of the prevention programmes this organisation provides to the community are liaisons with public schools, providing workshops on addiction prevention and other types of interventions. As a result of the ongoing collaboration between CIJs and government funded schools, it was possible to contact public middle schools through Juvenile Inclusion Centres. The head of the research department in CIJ was contacted and a meeting was organised, where it was agreed CIJ would take part and provided support for the project. Before data collection started, it was required to register the project within their research department and undergo ethical approval procedure in the institution as well.

The school's sample from where data was collected was randomly selected. Once schools were identified, a member of the service approached the head teacher in schools to extend an invitation to participate in the project. Once the school agreed to participate, the principal researcher and the head teacher met. During the meeting the aims and objectives of the study were explained in detail as well as the procedure of data collection and permission was requested to contact students (See Figure 3.1).

Before contact with potential participants was made, the principal researcher explained the age range needed for the study to the school's headteacher to identify classrooms of students that were among that age range. Only classrooms in that age range were

approached. After permission from the head teacher was granted, dates and times were set taking into account timings and calendar of each school. Classrooms were selected according to the inclusion criteria, where students age range was from 15 to 19 years old. The principal researcher approached each classroom and explained in detail the aims and objectives of the study. It was clearly stated that their participation was completely voluntary, that there was no pressure to participate and that there would not be any consequences if they decided not to. Moreover, it was emphasized that all the information provided was confidential and anonymous. Lastly, if the students had questions regarding the study these were addressed by the principal researcher.

Twenty-four hours before the questionnaires were given to participants, an information sheet and an informed consent were provided. The following day, if students had agreed to participate, the questionnaires were handed in and completed. The principal researcher stayed in the classroom while the students completed the questionnaires and if they had any question or query, she approached each student individually. Completion of the questionnaires took the students approximately from 35 minutes to one hour. During the survey students were asked to sit by themselves on their own desk and were reminded that the questionnaires need to be answered individually, it was ensured participants had enough space and were seating separately to prevent copying or viewing each other's questionnaires. Moreover, the principal researcher gave the following statement during the initial informative talk to ensure participants completed questionnaires confidentially and without peer pressure.

> "One of the main things to remember is that all the information you provide is strictly confidential and anonymous, do not feel there is any

pressure to participate even if your classmates and friends decide to take part in the study. Your participation is completely voluntary and there will be no consequences if you decide not to take part."

It was decided that for better control of pressure to participate all students were advised to remain in the classroom even if they did not wish to participate in the study. The classroom teacher and the principal researcher gave instructions of other work students could do if they do not wish to complete the questionnaires. After the explanation the teacher was asked to leave the classroom, in some cases this was plausible and others this was not (some classrooms had much more disruptive students than others, therefore, sometimes the presence of the teacher was necessary in order to maintain group control). The principal researcher provided a booklet with the questionnaires to every student in the classroom. Afterwards, they decided individually if they wanted to complete or not the questionnaires without any of their classmates having to know. Each classroom comprised of 30 to 50 students depending on the school, grade and attendance.

3.3. Adolescent Substance Misuse Clinical Sample

3.3.1. Juvenile Inclusion Centres: Treatment Centres for Young People with Problematic Drug Use

There are different ways to start treatment in these centres. People can be self-referred, if anyone believes they have an issue with substance abuse they can attend to any centre and request details regarding treatment, there are also telephone lines where people can call. There are, however, other ways to be referred, for example when someone who has been incarcerated and their crime was motivated by or related with substance abuse

police might oblige them to get treatment in order to be eligible for and maintain parole. Another way to receive treatment is through health services. When a patient presents to a health clinic reporting substance abuse, the Dr might suggest them to get treatment at CIJ. Treatment services were selected alongside the head of the research department of Juvenile Inclusion Centres. The first three centres selected were CIJ Gustavo A. Madero Aragon, CIJ Tlanepantla and CIJ Iztapalapa Poniente. Two main reasons played part in the selection of these centres, firstly, it was identified which centres had the most available population in the age range of the study and, secondly, the availability of each centre.

The names of the before mentioned centres include the name of the borough where they are located in. The first centre contacted was CIJ Gustavo A. Madero Aragón, located in the borough Gustavo A. Madero, where a total of 1,164,77 people resides. The crime rate in this borough is relatively high, with 10% of all crime committed in Mexico City, this borough holds the 3rd place in insecurity (the borough with the highest reported crime rate is Cuauhtémoc with 15%) (Justicia, 2018) (See Figure 3.2).

3.3.1.1. Boroughs' Description

CIJ Iztapalapa Poniente and CIJ Iztapalapa Oriente are located in the borough of Iztapalapa with a total 1,827,868 habitants, this borough has the largest population in Mexico City. It is characterised by having one of the least developed infrastructures in the city with important deficits in access to clean drinking water. One of the main problems in this borough located east of Mexico City are the high rates in crime, being the second most dangerous borough with 14% of all crimes in the city committed here; it has the highest rates of drug trafficking, violence against women, and traffic of stolen

auto-parts (Justicia, 2018). CIJ Tlanepantla is located in the borough Tlanepantla in Estado de Mexico is one of the 125 boroughs in this county. With a total population of 700,734 is one of the most industrialised boroughs (INEGI, 2015).

After a couple of months collecting data from these centres it was observed that while they were very effective in providing participants for the school sample, they did not have enough flow-through of patients for the clinical sample. Therefore, the principal researcher contacted the head of the research department to suggested new centres to collect data from; CIJ Tlalpan and CIJ Iztapalapa Oriente. This decision was made after reviewing a patient report from JIC from 2015 where it was observed that those centres had more patients in the age range needed and where the main substance of abuse was cannabis. CIJ Tlalpan, located in Tlalpan borough, is the borough with the largest km in Mexico City, however its population is smallert than the other boroughs, with only 667,104 residents. Regarding insecurity and crime, this borough accounted for 5.7% of offences in the city (Justicia, 2018).

Ecatepec de Morelos is the most populated borough in Estado de Mexico with 1,677,678 people. It is the second most populated borough in the country after Iztapalapa (INEGI, 2015). Ecatepec is considered the most dangerous borough in Estado de Mexico and one of the most dangerous in the country, with extremely high rates of crime including homicides, kidnaping, sexual assaults and home, business and car robbery (Justicia, 2018). Moreover, this borough has a permanent gender alert as it is the borough where more “feminicidios” (violent homicides against women) occur in the country (Gobernacion, 2018). In 2015 it was considered the borough with the highest rates of extreme poverty in the country (INEGI, 2015).

3.3.2. Adolescent Substance Misuse Clinical Sample: Recruitment and Sampling

Before contact with potential participants was made, the principal researcher explained the inclusion criteria to the service personnel (age range 13 to 19-year olds, primarily cannabis users) to request their support with identifying potential eligible participants. Once personnel helped with the identification of participants that met the inclusion criteria, they were approached. The method of approach could differ depending on the service. In every service the above-mentioned strategy was used, however in some services an introductory talk was provided to all new patients on a particular day during the week. When a service provided this talk the principal researcher would participate in it, explaining the aims and inclusion criteria. By the end of the talk, if there was anyone interested in participating, they were advised to approach the researcher for further information and, if they agreed, complete the questionnaires.

To ensure participants completed all questionnaires confidentially and without any pressure, the principal researcher gave the same statement to participants in the substance misuse clinical sample than in the school sample, excluding the part when specifying participation of "classmates".

The principal researcher arranged a specific day during the week to attend to each service, depending on the activities and the day of the week each service held the introductory talk. Once participants were approached, the aims and objectives of the study were explained, reassuring that all the information provided is anonymous and that there is no pressure to participate, it is completely voluntary and there will be no

consequences if they decide not to take part in the study. If the participants had questions regarding the study, those were answered by the principal researcher.

Finally, an information sheet and an informed consent were provided and, questionnaires were administered in small groups by the principal researcher which took approximately 30 minutes to complete. During the assessment participants were seated separately one from another and were reminded to answer the questionnaires individually. When participants had questions or did not understood some of the items in the questionnaires, they approached the principal researcher for clarification.

3.4. Questionnaires

Participants in both the school sample and the substance misuse clinical sample, completed identical questionnaires describing patterns of cannabis use, psychotic-like experiences and associated factors. Questionnaires are described in detail below.

3.4.1. Cannabis Use Questionnaire

Cannabis use was assessed with a series of questions regarding lifetime, past six months, age of onset, amount, method and frequency of use.

1. Have you ever used cannabis?
2. Have you used cannabis in the last 6 months?
3. How old were you when you first tried cannabis?
4. How many joints do you smoke on a typical occasion (1/4 of a joint, ½ of a joint, one, two, three, four or more)?

   This was recoded into a two-category variable for analysis and categories were defined as less than one or one and two or more.

5. Do you mainly use cannabis (in a joint with tobacco, in a joint without tobacco, in a bong or waterpipe, eaten, e-cigarettes, other)?
6. How often do you use cannabis (every day or almost daily, once or twice a week, once or twice a month, less than once a month, once or twice a year, only tried it once)?

   The primary variable of frequency of cannabis use was structured as a 6-category variable.
7. Do you mainly use cannabis alone or socially (with friends)?

Moreover, additional questions regarding type of cannabis mainly used, type of cannabis they preferred to use and type of cannabis most available to them were included (i.e. herbal cannabis, hydroponic, redhead or skunk, hash or resin).

8. Which of the following best describes the type of cannabis you mainly use?
9. Which of the following best describes the type of cannabis that is most available for you to use?
10. If you could choose one, which of the following would you prefer to use?
    1. Herbal cannabis
    2. Hydroponic, redhead or skunk
    3. Hash or resin
    4. Don´t know

This was assessed by providing pictures of different types of cannabis to have more accurate responses from participants regarding the type of cannabis they use.

Herbal Cannabis

Hydroponic,

redhead or skunk

Hash or resin

The cannabis use questionnaire was previously used to survey a general adolescent population sample of 467 adolescents (mean age 16.8) in UK secondary schools (Mackie, et al. under review), but subsequently adapted for use with adolescents in Mexico. There is no standardised questionnaire that examines types of cannabis in adolescents; however similar formats (self-report) have been used before (Di Forti et al., 2014; Freeman & Winstock, 2015; Wilson, Freeman, & Mackie, 2019). Piloting among an adolescent Mexican sample was conducted months prior to the start of data collection; items are described in the Appendix.

During data collection, some participants had queries regarding amount of cannabis mainly used, as they mentioned that they did use cannabis, but not in a joint. The principal researcher addressed this and requested participants to answer thinking of the average amount used and convert that into one of the given options. However, it was identified that the lack of a standard unit measure makes this assessment difficult, and it is difficult for participants to identify or calculate the exact number of grams using in each joint or in pipes and bongs.

3.4.2. Cannabis Experience Questionnaire

This scale was structured from the Cannabis Experiences Questionnaire (CEQ) which was developed by Barkus et al. in 2006, this questionnaire assesses the subjective effects of cannabis use and it is structured of 3 different subscales; pleasurable experiences, psychosis-like experiences and after-effects (Barkus, 2006). For brevity and in order to facilitate data collection four items assessing psychotic-like experiences and three items assessing after-effects were extracted from two subscales in the CEQ. The items attempt to quantify the effects experienced after the use of cannabis which are associated with anhedonia (characterised by users reporting feeling lack of motivation, passive and non-productive), cognition and psychotic-like experiences. The scale is formed by the following items:

Have you experienced any of the following effects after smoking cannabis? Please choose only one option.

A. Feelings of paranoia or suspiciousness
B. Hearing voices
C. Feeling like I am going crazy/mad
D. Not wanting to do anything, lack of motivation
E. Difficulty in concentrating
F. Not able to think clearly
G. Seeing visions
H. Other: please specify

Each of these potential after-effects were rated on a four-point scale: (1 = rarely or never, 2 = time to time, 3 = more often than not, 4 = almost always). Responses to the

eight questions were summed to form a single scale representing the extent to which participants reported experiencing negative effects after using cannabis.

3.4.3. Psychotic-Like Experiences: The PRIME Screen Questionnaire for Prodromic Symptoms

This questionnaire was elaborated by McGlashan, T. et al. by combining the Structured Interview of Prodromal Syndrome and an in-depth interview. The main objective was to develop a scale that could be used in the general population that measured prodrome symptoms (first signs, prior to the development of a psychotic disorder) which was not available then. The Spanish translation and reliability were conducted in Mexico City with a sample of 532 adolescents from 15 to 23 years old (Fresan, Apiquian, Ulloa, & Nicolini, 2007). With 12 items the approximate time of completion is from 10 to 20 minutes. The internal consistency of the scale was of 0.88. To the best of my knowledge, this is the only questionnaire examining psychotic-like experiences translated (English to Spanish) and validated in adolescent Mexican population, which provides reassurance that the instrument is measuring psychotic-like experiences in the population recruited.

3.4.3.1. The PRIME Screen Questionnaire for Prodromic Symptoms: Items

1. I think that I have felt that there are odd or unusual things going on that I can't explain.
2. I think that I might be able to predict the future.
3. I may have felt that there could possibly be something interrupting or controlling my thoughts, feelings or actions.

4. I have had the experience of doing something differently because of my superstitions.
5. I think that I may get confused at times whether something I experience or perceive may be real or may be just part of my imagination or dreams.
6. I have thought that it might be possible that other people can read my mind, or that I can read other's mind.
7. I wonder if people may be planning to hurt me or even may be about to hurt me.
8. I believe that I have special natural or supernatural gifts beyond my talents and natural strengths.
9. I think I might feel like my mind is "playing tricks" on me.
10. I have had the experience of hearing faint or clear sounds of people or a persona mumbling or talking when there is no one near me.
11. I think that I may hear my own thoughts being said out loud.
12. I have been concerned that I might be going crazy.
13. Have you ever seen something or someone that other people could not see?

The PRIME Screen Questionnaire was rated in a 6-point rating scale (1=completely disagree, 2=disagree, 3=somewhat disagree, 4=not sure, 5=somewhat agree, 6=completely agree).

A further item to examine visual hallucinations was added as prior research indicate that these experiences are part of the continuum and may be of interest to analyse (van Gastel et al., 2012).

- Have you ever seen something or someone that other people could not see? (Visual hallucinations). This item was also assessed on the same six-point scale described above.

Moreover, four items were added to the original scale. These items were added in order to obtain more detailed information of the participants experiences and if these occurred under the influence of any drug. The items added were the following:

- How old were you the first time you experienced this symptom?
- Did this symptom occur after using drugs? If it did,
    - Which drug?
- Did you ever experience this symptom without the use of any drug?

3.4.4. Demographic Questions

- Age (years)
- Gender (male, female)
- Ethnicity

Firstly, ethnicity was categorised as follows: “Caucasian”, “Hispanic or Latin”, “African-American”, “African-Mexican”, “Asian” and “Other”. Categories were identified when running the frequencies of the original variable. Afterwards, the main categories identified and selected for the following analyses were “Hispanic or Latin”, “Caucasian” “African Descent” and “Other”. Ethnicity was recoded as a 4-category variable instead of a 6-category variable.

3.4.5. Socioeconomic Questionnaire

Socioeconomic level was assessed by using a questionnaire developed by the Marketing and Opinion Intelligence Mexican Association which is based on a statistical model which categorise Mexican homes in different levels according to their capacity to fulfil basic requirements of families (Asociación Mexicana de Agencias de Inteligencia de Mercado y Opinión, 2108). In the following page, next to each question of the questionnaire, the value, depending on the answer of the participant, can be found.

1. How many rooms does your house have? Please do not include bathrooms, half bathrooms, hallways or courtyards. (1 = 0; 2 = 0; 3 = 0; 4 = 0; 5 = 8; 6 = 8; 7 or more = 14).
2. How many complete bathrooms with shower and W.C. are in the house for exclusive use of your family? (1 = 16; 2 = 36; 3 = 36; 4 or more = 52).
3. Does your home have a functioning shower in any of the bathrooms? (No = 0; Yes = 10).
4. Considering all the lightbulbs that you and your family use to light your house, including ceilings, walls, bed lamps or floor lamps, how many lightbulbs are there in your house? (0-5 = 0; 6-10 = 15; 11-15 = 27; 16-20 = 32; 21 or more = 46).
5. The floor in your house is predominantly soil, cement or other type of material? (Soil or cement = 0; Other type of material = 11).
6. How many cars do your family own, excluding taxis? (0 = 0; 1 = 32; 2 = 41; 3 or more = 58).
7. Does your home have a gas or electric stove? (No = 0; Yes = 20).
8. Thinking about the family member that contributes the most economically in your house, which was the last year of studies he/she completed? (Did not study

= 0; primary not completed = 0; primary completed = 22; secondary school not completed = 22; secondary school completed = 22; commercial degree = 38; technical degree = 38; high school not completed = 38; high school completed = 38; undergraduate not completed = 52; graduate completed = 52; diploma or Master = 72; PhD = 72).

3.4.5.1. Scores and Levels

The following are the different socioeconomic levels depending on the score they had. Scores are calculated by adding the numbers in parenthesis above, depending on the answer. Levels are categorised as A/B, C+, C, C-, D+, D, E.

- A/B: (193+) Highest living standards in the country, all needs are covered, and it is the only sector with resources to invest and plan ahead. Only 3.9% of homes in Mexico have this living standard.
- C+ (155 – 192) All needs are covered; however, there might be difficulties to invest, save and plan ahead. Comprised by 9.3% of households in the country.
- C (128 – 154) Practical living standard with certain commodities; however, basic in entertainment and technology. They comprise 10.7% of the country's households.
- D+ (80 – 104) Minimum sanitary home infrastructure in the house, 19% households in the country.
- D (33 – 79) Might have a property but lack basic services like running water or gas. Comprised by 31.8% of households in the country.
- E (0 – 32) Least quality of life and do not have any services (water, gas, electricity). Constitutes 12.5% of households in Mexico.

Initially, the variable was coded as a seven-category variable, however for further and more specific analyses it was recoded into a three-category variable. Categories were clustered according to the original questionnaire where the most similar levels were combined:(A/B) as one, (C+/C/C-) as two and (D+/D/E) as three.

3.4.6. Use of Other Drugs

As part of the questionnaires included in the present study, a systematic questionnaire regarding use of other drugs was administered. Research has continuously shown that cannabis use is associated with use of other drugs, licit and illicit (Hall, 2014), therefore the interest of including this questionnaire. Furthermore, it has been found that psychotic-like experiences and use of other drugs are significantly associated (Barkus & Murray, 2010; Shevlin et al., 2017). This questionnaire assessed use of:

- Tobacco
- Alcohol
- Cocaine
- Crack
- Solvents
- Hallucinogens
- Ecstasy
- Benzodiazepines / Sleeping Pills
- Opioids (Not heroin, pain killers, etc.)
- Heroin
- Opium
- Amphetamines / Methamphetamines
- Other Drugs (Legal Highs, etc.)

Use of other drugs was assessed through specific questions regarding:

1. Lifetime use (Yes/No)
2. Age of first use (Years)
3. Frequency of use: every day or almost every day; once or twice a week; once or twice a month; less than once a month; once or twice a year; only tried it once.

A guide to help identification was provided when requested to participants who did not know or were not sure of what each substance was. This guide included pictures and "common" or drug street names and examples, see the Appendix.

3.5. Statistical Analysis

This cross-sectional study in an adolescent student sample and adolescent substance misuse clinical sample (primarily cannabis users) examined the relationship between cannabis use and psychotic-like experiences. Data from the school sample were analysed separately from the clinical sample data. All analyses were conducted using the statistical package IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.

The main independent variable was cannabis use and the main outcome variable was psychotic-like experiences (continuous); however, the following covariates were also included in the analyses:

1. Age
2. Gender
3. Sociodemographic characteristics
4. Use of other drugs

For statistical analyses, the following approaches were used. The principal dependent variable was psychotic-like experiences, assessed using the PRIME screen questionnaire. While the primary interest was the association between psychotic-like experiences and cannabis use, potential confounding covariates (i.e. age, gender, other drug use, and sociodemographic characteristics) were also assessed and included in the statistical models. My primary analytic approach involved the use of regression models. The variable psychotic-like experiences was conceptualized as a continuous variable (e.g., number of symptoms experienced), in which case linear regression analysis was conducted. Age, gender, sociodemographic characteristics and use of other drugs were included in each model. Statistical analyses are described below. Firstly, descriptive statistics were performed to explore prevalence of lifetime cannabis use by age, gender, ethnicity and socioeconomic status.

Descriptive statistics were conducted to identify number of participants by age and gender, ethnicity and socioeconomic status. Analyses were conducted to identify mean age of onset of cannabis use, frequency and quantity of use, type of cannabis mainly used and preferred route of administration. Furthermore, chi-square analyses were conducted to identify differences between the before mentioned variables and sociodemographic characteristics.

3.5.1. Patterns of Cannabis Use

Analyses were conducted to identify differences in patterns of cannabis use and age, gender, age by gender interaction, ethnicity and socioeconomic status. Use of different types of cannabis among participants were examined using three different variables: the type of cannabis mainly used, the type of cannabis preferred by users and finally the

most available type of cannabis. The original categories included in the analysis were: herbal cannabis, skunk, hydroponic or redhead, hash or resin and don't know. Prevalence of main type used, preferred type and most available type of cannabis were reported. In order to identify statistically significant differences in type of cannabis mainly used by age, gender, age by gender interaction, ethnicity and socioeconomic level chi-square analyses were performed.

Prevalence of routes of administration were also analysed. The variable in the questionnaire comprised of 6 different categories, however, for further analyses the variable was recoded into a dichotomous measure assessing use in a bong or water pipe vs. any other. Analyses were conducted to identify significant differences by age, gender, age by gender interaction, ethnicity and socioeconomic status. To assess preference of participants between social or non-social use of cannabis participants were asked if they mainly used cannabis alone or with friends. Prevalence of use was reported, and differences were assessed with the dichotomous variable of social or non-social use and all the sociodemographic characteristics previously described.

3.5.2. Psychometric Properties of the Cannabis Experience Questionnaire and Differences by Sociodemographic Characteristics and Use of Other Drugs

Principal components analysis was conducted on the seven items of the after-effects scale. The internal consistency in the scale was measured by Cronbach's Alpha. Analyses of variance were conducted to identify if the total score of the cannabis experience questionnaire varied by age, gender, ethnicity and socioeconomic status. Linear regression analyses were performed to identify differences between the total

scores of the questionnaire while controlling for age of first use, age, gender and frequent or non-frequent use.

3.5.3. Use of Other Drugs

Analysis of prevalence of lifetime use, age of first use and frequency of use of other drugs were conducted. Both licit and illicit drugs were assessed, and descriptive statistics reported. Next a series of analyses were conducted to examine the associations between lifetime cannabis use and measures of use of other drugs.

3.5.4. Associations between Patterns of Cannabis Use and Use of Other Drugs

Analyses were conducted to identify associations between different patterns of cannabis use and use of other drugs in both samples.

3.5.5. Associations between Different Patterns Cannabis Use, Sociodemographic Characteristics and Use of Other Drugs

In order to identify differences between the continuous measure of cannabis use, sociodemographic characteristics and the use of other drugs analyses of variance were conducted. Different dichotomous measures of cannabis use (lifetime use, at least monthly use and type of cannabis mainly used) were employed to explore any associations with sociodemographic characteristics and use of other drugs. Odds ratios obtained from crosstabs, chi-square and logistic regression analyses were conducted. Furthermore, hierarchical regression models were conducted to identify the level of association between different patterns of cannabis use, sociodemographic characteristics and use of other drugs, while taking into account all variables. Firstly, sociodemographic variables were entered followed by use of other drugs, both licit and

illicit. Measures of psychotic-like experiences were not entered at this point of the analyses.

3.5.6. Psychotic-Like Experiences

In order to identify correlations between variables and to examine consistency of the questionnaire, principal component factor analysis and reliability analysis were performed to the PRIME Screen Questionnaire. Mean scores of each item of the were analysed, followed by descriptive statistics to identify prevalence of psychotic-like experiences by age and gender.

3.5.7. Associations between Psychotic-Like Experiences, Sociodemographic Characteristics and Use of Other Drugs

For the psychotic-like experiences analyses, in addition to the continuous measure of the total score of the PRIME Screen Questionnaire, a dichotomous measure was created (Yes/No Presence of PLE's). Previous literature showed feasible to create a dichotomous outcome on the PRIME Screen Questionnaire (Kobayashi et al., 2008). In the version of the questionnaire used for this study a 40+ score would result in scoring as positive in the psychotic-like experiences assessment.

For the continuous measure of the PRIME Screen questionnaire, analyses of variance were conducted to identify differences between psychotic-like experiences, sociodemographic characteristics and use of other drugs. Furthermore, similar to the analyses conducted with cannabis use, hierarchical regression analyses were conducted to identify the association between psychotic-like experiences, sociodemographic

characteristics and use of other drugs. The final model was fitted to consider all variables, except for cannabis use.

3.5.8. Patterns of Use of Other Drugs and Associations between the Use of Other Drugs and Psychotic-Like Experiences

Descriptive statistics were conducted to determine prevalence of psychotic-like experiences, overall and by gender. Furthermore, analyses were conducted to identify if use of other drugs were independently associated with psychotic-like experiences. Cross-tables were created to identify prevalence of use and odds ratio between psychotic-like experiences and daily and weekly use of tobacco; daily, weekly and monthly e-cigarette use; daily and weekly alcohol use; every day and weekly binge drinking; daily, weekly and monthly benzodiazepine use; daily, weekly and monthly methamphetamine use and daily, weekly and monthly solvent use.

3.5.9. Multiple Regression Analyses: Association between Cannabis Use and Psychotic-Like Experiences Controlling for Sociodemographic Characteristics and Use of Other Drugs

Lastly, hierarchical multiple regression analyses were conducted to identify associations between different patterns of cannabis use and psychotic-like experiences while controlling for sociodemographic characteristics and use of other drugs; these analyses are the main interest of the present study. Models were conducted with measures of cannabis use as main predictor, followed by sociodemographic characteristics and use of other drugs. The outcome variable was psychotic-like experiences.

3.6. Ethical Considerations

The ethics application for this study was submitted on the 31st of October 2017. The approval was granted on the 18th of December 2017 by the Psychiatric, Nursing and Midwifery Research Ethics Subcommittee. Study Reference Number: HR-17/18-5256. The project was registered at Juvenile Inclusion Centres and their Ethics Committee reviewed the project in order to start data collection. This process started in December 2017 and approval was granted in February 2018. Study Reference Number: 203-17. Questionnaires were anonymous and were only identified with previously assigned identification numbers. Documents do not contain personal data that may jeopardize confidentiality. Documents that might contain the participants' name are the informed consents which are kept separate from the questionnaires.

3.7. Power Analyses

Power estimates were conducted in Gpower; each analysis took into consideration data extracted from studies regarding cannabis use and psychotic-like experiences in adolescent populations relevant to the present study.

3.7.1. Adolescent Student Sample

In the school setting with a sample size of N=500 participants, from which it is estimated that 30% (n=150) will be cannabis users and 70% (n=350) are non-cannabis, users based on the survey conducted in 2015 by Villatoro, et al. in Mexico City (Villatoro et al., 2015). I assume based on a systematic review and meta-analysis that the prevalence of psychotic-like experiences in non-cannabis users will be approximately 7.5% (Kelleher et al., 2012). Under these assumptions my proposed sample size of 500 participants will have .90% power to detect an odds ratio of 1.8 between cannabis and non-cannabis users as statistically significant.

3.7.2. Adolescent Substance Misuse Clinical Sample

In the clinical setting, based on a meta-analysis conducted in 2016 by Marconi, A. et al., the estimated prevalence of psychotic-like experiences in cannabis users will be 30% (Marconi et al., 2016). Under this assumption my proposed sample size of 120 will have .90% power to detect and odds ratio of 3.5 between severity of cannabis use and psychotic-like experiences (Faul, Erdfelder, Buchner, & Lang, 2009).

3.7.3. Missing Data

Out of 198 participants reporting lifetime cannabis use between 3 and 7 had missing data in frequency, quantity, method and type of cannabis mainly used, 1.5 to 3.5% of the sample, which is a small percentage of the 198 participants. Thirty participants had missing data on the total score of psychotic-like experiences 4.6% of the sample. To explore whether cannabis use predicted missing data on the PRIME Screen Questionnaire logistic regression analyses were conducted, results showed no significant associations between cannabis use and missing data (OR=1.29, 95%CI=.59-2.85). Among sociodemographic characteristics, gender was the only variable associated with missing data, indicating that males were more likely to not respond in the psychotic-like experiences questionnaire (OR=2.18, 95%CI=1.00-4.77).

3.8. Sample Description

3.8.1. Adolescent Student Sample

A total 657 participants among the age of 15 to 19-year olds completed the questionnaires. For data analysis 648 were included (participants excluded as age range criteria was not met). Fifty-three percent of the sample were females and 47% males. The mean age of the school sample was 16.51 (SD =1.05) and the median 17. The

response rate of the school sample was 95% as students were happy to participate. Regarding ethnicity, participants mainly indicated Hispanic or Latin as their ethnicity with 60.2% identifying themselves in this category, followed by African-Descent with 25.3%, followed by 6.5% as Caucasian and 6% as Other. Regarding socioeconomic level in the school sample 62% scored as being part of level C+/C/C-, followed by 21.9% in level D+/D/E and 16% in socioeconomic level A/B.

3.8.2. Adolescent Substance Misuse Clinical Sample

A total of 121 participants seeking treatment for problematic cannabis use, in the age range of 13 to 21-year olds completed the questionnaires. Participants were included if they reported cannabis as the primary drug of abuse, however they could also report use of other drugs. A total of 84.3% were male and 14.8% were female. The mean age of participants was 16.56 (SD=1.58) and the median age was 17. The response rate of the clinical sample was higher than the school sample, with 99% of participants approached and recruited accepting to participate and completing the questionnaires. Regarding ethnicity, 48.7% identified themselves as Hispanic or Latin, 24.3% as African-Descent, 5.2% as Caucasian and 20% as Other. Regarding socioeconomic level, 16.5% scored in socioeconomic status A/B, 51.3% in C+/C/C- and 32.2% in D+/D/E.

Figure 3.1 Adolescent Student Sample: Consort Diagram Data Collection

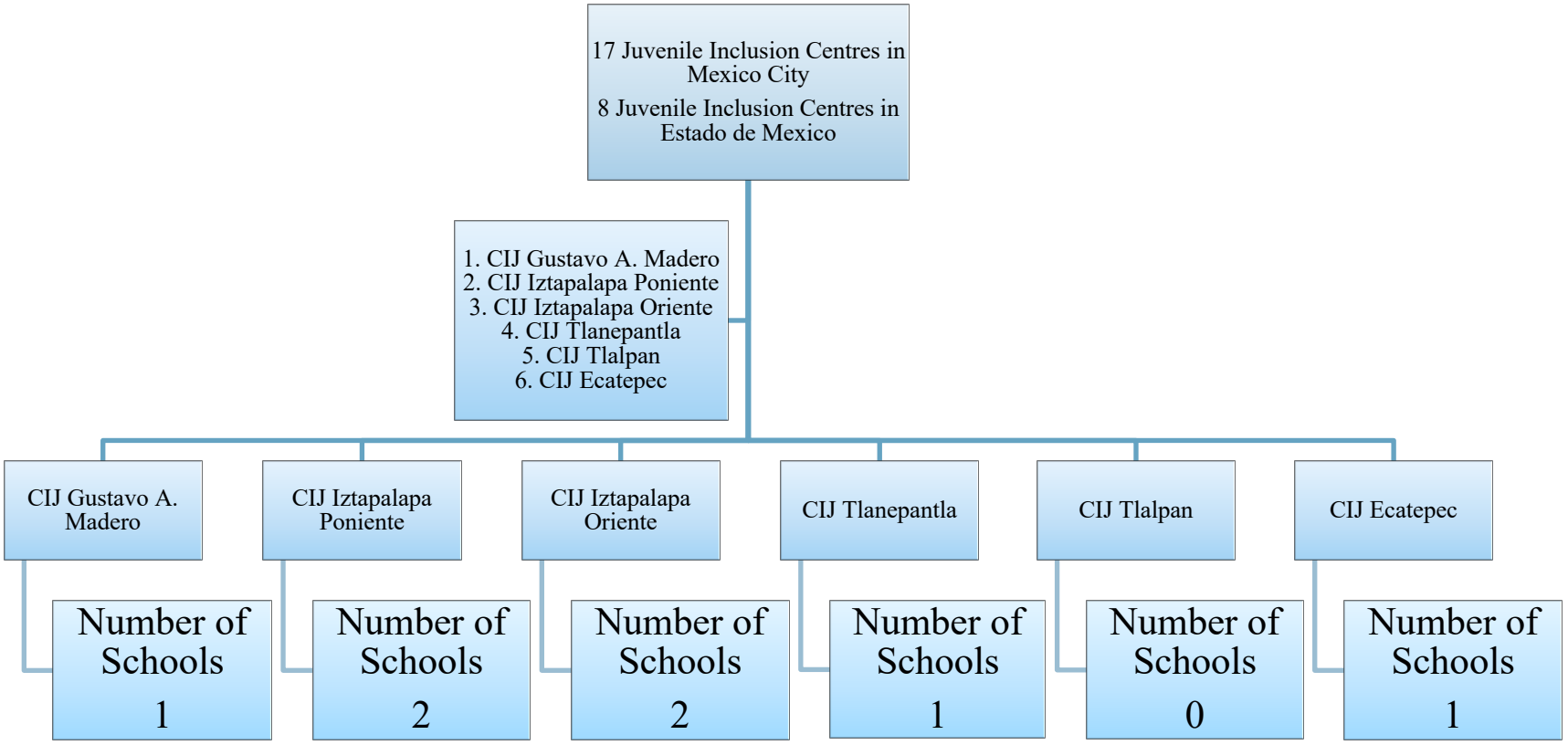
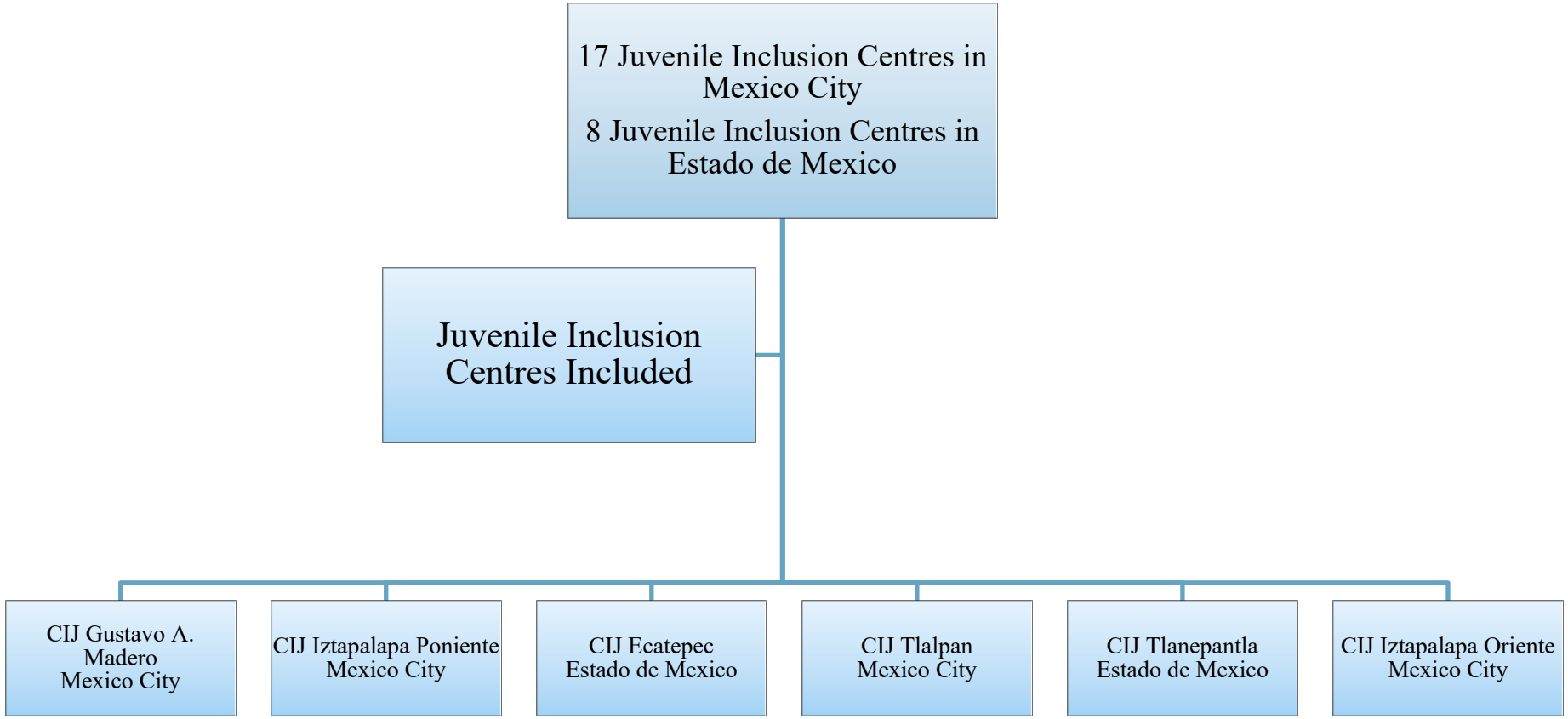


Figure 3.2 Adolescent Substance Misuse Clinical Sample: Consort Diagram Data Collection



4. Patterns of Cannabis Use and Associated Factors in a Sample of School Students in Mexico City

4.1. Introduction

Cannabis use in the general population in Mexico has shown a steady increase in the last decade (Villatoro, 2017). It is the most commonly used illicit drug among adolescent students (14 to 19 years old) with 19.6% lifetime prevalence of use (Villatoro et al., 2015). High levels of cannabis use have not been seen exclusively in Mexico, in the United Kingdom in 2018 the prevalence of lifetime cannabis use was of 30.7% among 16 to 24 year olds (Flatley, 2018). In the United States 15.3% of adolescents from 12 to 17 years old reported lifetime cannabis use in 2017 (CBHSQ, 2017), however, contrary to what is seen in Mexico, prevalence of cannabis use in these countries is not increasing as rapidly.

Despite the increase of prevalence of use and global changes in attitudes around legalisation (McGinty et al., 2017), research continues to show the adverse effects of cannabis use in both, adolescents and adults (Bloomfield et al., 2019; Hall et al., 2019). Furthermore, research has shown that early onset of cannabis use during adolescence, compared to later onset of use, may be detrimental to brain structure and cognitive function (Solowij, 2015).

During adolescence, the brain is still undergoing development of neurological connections (Winters, 2011) and this might confer vulnerability when using drugs. Research has shown that some of the different repercussions adolescents may experience when using cannabis, include decreased executive functions (Gorey et al., 2019) impairments in memory, attention, and learning, and many deficits persist after 3

to 4 weeks of abstinence (Lubman et al., 2015). Furthermore, Gorey et al. examined whether the relationship between cannabis use and cognition differed between adolescents and adults in both, rodents and humans and it was found that, in humans, impairment was more sever in adolescent frequent and heavy cannabis users than in adults with the same patterns of use (Gorey et al., 2019), however, authors mention the need for further studies to support these findings.

Despite these concerns there has been relatively little research into patterns of cannabis use and physical and mental health among adolescents in Mexico. While previous research has demonstrated a recent increase in the prevalence of cannabis use among adolescents in Mexico, less is known about patterns of use and adverse effects, e.g. mental health problems, executive function impairments and use of other drugs. Therefore, this Chapter addresses a number of important gaps in our understanding of cannabis use among adolescents in Mexico. In particular: age of first use of cannabis, types of cannabis (herbal cannabis, skunk, hydroponic, redhead or hash or resin) mainly used, preferred type and most available type and the assessment cannabis experience questionnaire. In addition, use of other drugs (licit and illicit) was assessed and this chapter reports associations between cannabis use and the use of these drugs.

4.2. Objectives

1. To identify the prevalence and extent of cannabis use among 15 to 19-year-old students in Mexico City and Estado de Mexico. Patterns of cannabis use to be examined include measures of lifetime use, frequency, quantity, routes of administration and social or non-social use.

2. To examine potential sociodemographic differences in prevalence and extent of cannabis use. Sociodemographic factors include age, gender, ethnicity and socioeconomic status.
3. To identify type of cannabis (high-potency, low-potency) mainly used, preferred and most available.
4. To describe lifetime prevalence, age of first use and frequency of use of other drugs (licit and illicit) among the complete sample and specifically in cannabis users; and to identify potential differences in frequency of use of other drugs according to use or non-use of cannabis.
5. To analyse the reliability of the cannabis experience questionnaire, to identify the mean scores and examine potential differences by patterns of cannabis use and sociodemographic characteristics.

4.3. Methods

Results presented in this chapter are based on the analysis of data collected from 648 school students aged 15 to 19 years old who completed questionnaires on their patterns of cannabis use. A full detailed description of the procedures used for data collection has been provided in Chapter 3. Questionnaires were employed to collect data regarding participants' use of cannabis, sociodemographic characteristics, a cannabis experience questionnaire (Barkus, 2006) and a specific questionnaire assessing use of other illicit and licit drugs.

4.4. Statistical Analysis

4.4.1. Cannabis Use

All analyses were conducted using the statistical package IBM SPSS Statistics Version 25, Release 25.0.0.1 64-bit edition. Descriptive statistics were performed with crosstabs to identify the prevalence of lifetime cannabis use by age, gender, ethnicity and socioeconomic status. To ensure required assumptions to conduct regression-based statistical analyses were met I conducted to following checks.

1. Linearity and additivity
2. Statistical independence
3. Homoscedasticity
4. Normality

Chi-square and logistic regression analyses were conducted to identify significant differences and associations in frequency of cannabis use by age, gender, age by gender interaction, ethnicity and socioeconomic status. Similarly, these analyses were conducted to identify significant differences in quantity of cannabis use by age, gender, age by gender interaction, ethnicity and socioeconomic status.

Use of different types of cannabis among participants was assessed using three different variables, type of cannabis mainly used, type of cannabis preferred by users and most available type of cannabis. The original categories of these variables included in the analyses were: herbal cannabis, skunk, hydroponic or redhead, hash or resin and don't know. Prevalence of main type used, preferred type and most available type of cannabis were reported by participants. Chi-square and logistic regression analyses were conducted to identify statistically significant differences and associations in type of

cannabis mainly used by age, gender, age by gender interaction, ethnicity and socioeconomic status.

Prevalence of routes of administration (method of use) were also analysed. The variable in the questionnaire comprised of 6 different categories, however, for further analyses the variable was recoded into a dichotomous variable (bong or water pipe vs. any other). Chi-square and binary logistic regression analyses were carried out to identify significant differences and associations by age, gender, age by gender interaction, ethnicity and socioeconomic status. Furthermore, to assess preference between social or non-social use of cannabis participants were asked if use of cannabis was mainly alone or with friends. Prevalence of use was reported, and differences and associations were assessed using chi-square and logistic regression analyses with the dichotomous social variable and all the sociodemographic characteristics previously described.

4.4.2. Psychometric Properties of the Cannabis Experience Questionnaire

Principal components analysis was conducted on the seven items of the cannabis experience questionnaire and Cronbach's Alpha was conducted to assess the consistency of measure. Analyses of variance were conducted to identify if the total scores varied by age, gender, ethnicity and socioeconomic status. Moreover, patterns of cannabis use were analysed alongside the total score of the cannabis experience questionnaire scale to identify statistically significant differences among different patterns of cannabis use and the total score of the scale. Linear regression analyses were run to identify differences between the total scores of cannabis experience questionnaire while controlling for age of first use, age, gender and frequent or non-frequent use.

4.4.3. Use of Other Drugs

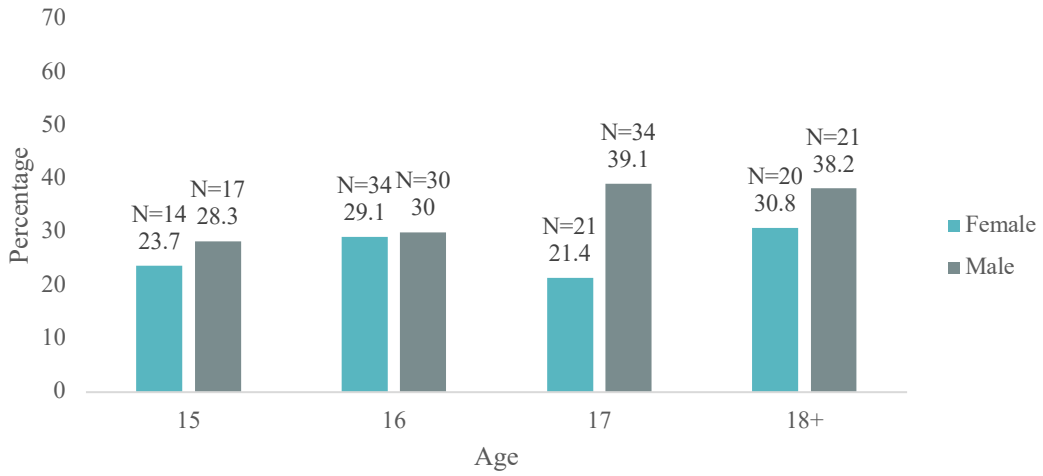
Analysis of prevalence of lifetime use, age of first use and frequency of use of other drugs were conducted. Both licit and illicit drugs were assessed, and descriptive statistics reported. Next, a series of analyses were conducted to examine the associations between lifetime cannabis use and patterns of use of other drugs including lifetime use, age of onset and frequency of use. The strength of the associations between different patterns of cannabis use and patterns of use of other drugs were assessed using odds ratios obtained from crosstabs.

4.5. Results

4.5.1. Prevalence of Lifetime Cananbis Use by Age and Gender

Just under one third of the school student sample (N=192; 29.6%) reported using cannabis at least once in their lifetime. Mean age of fist use of cannabis was 14.4 years old. Figure 4.1 shows the prevalence of lifetime cannabis use by age and gender. Logistic regression analysis indicated that there was no significant difference in prevalence of lifetime cannabis use by age (OR=.891, 95%CI=.751–1.056; p=.183). However, significant gender differences in prevalence of lifetime cannabis use were found (OR=.694, 95%CI=.494 –.975; p=.035), with prevalence of lifetime use being higher in males (N=102; 33.8%) than in females (N= 89; 26.3%). There were no significant differences in the interaction between age and gender on prevalence of lifetime cannabis use (OR=.864, 95%CI=.614 – 1.215; p=.401).

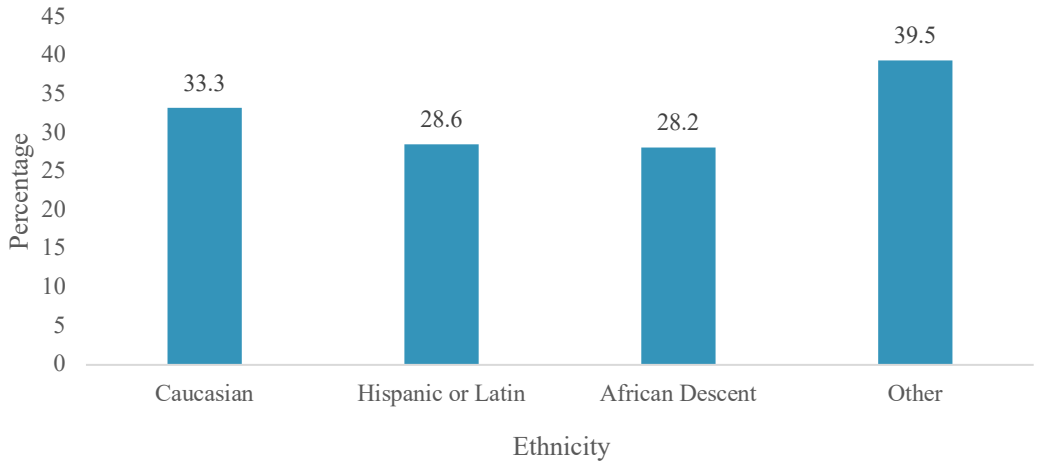
Figure 4.1 Prevalence of Lifetime Cannabis Use by Age and Gender



4.5.2. Prevalence of Lifetime Cannabis Use by Ethnicity

Chi-square analyses indicated that there were no significant differences in lifetime prevalence of cannabis use by ethnicity (χ^2=3.413, df=4, p=.491). Lifetime cannabis use was reported by 33.3% (N=14) of all participants identified as Caucasian, 28.6% (N=111) of all Hispanic or Latin, 28.2% (N=46) of participants who identified themselves as African-Descent and 39.5% (N=15) identified as Other.

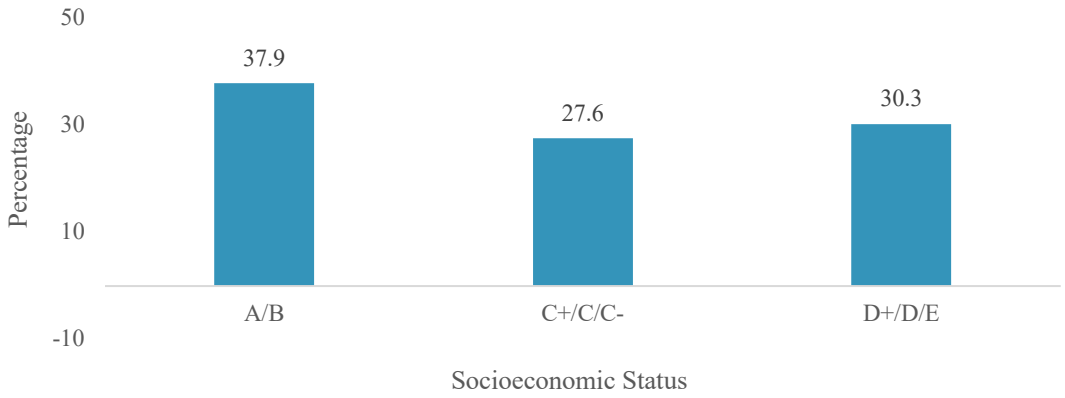
Figure 4.2 Prevalence of Lifetime Cannabis Use by Ethnicity



4.5.3. Prevalence of Lifetime Cannabis Use by Socioeconomic Status

There were no significant differences in the lifetime prevalence of cannabis use by socioeconomic status (χ^2=4.166, df=2, p=.125). Thirty-seven-point nine percent (N=39) of participants in socioeconomic level A/B reported lifetime cannabis use, followed by 30.3% (N=110) of participants in level D+/D/E and lastly, 27.6% (N=43) of participants in socioeconomic level C+/C/C-.

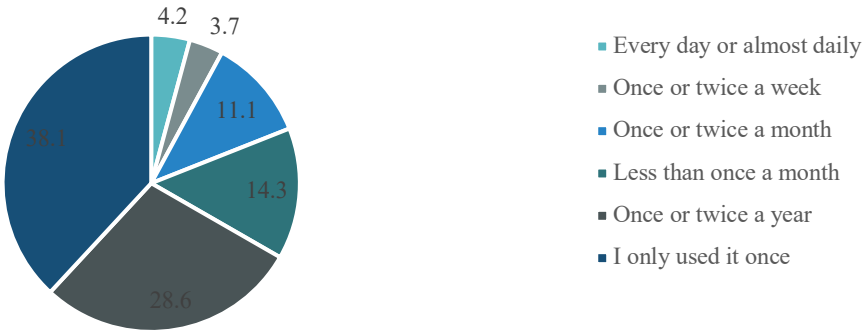
Figure 4.3 Prevalence of Lifetime Cannabis Use by Socioeconomic Level



4.5.4. Prevalence of Frequent Cannabis Use

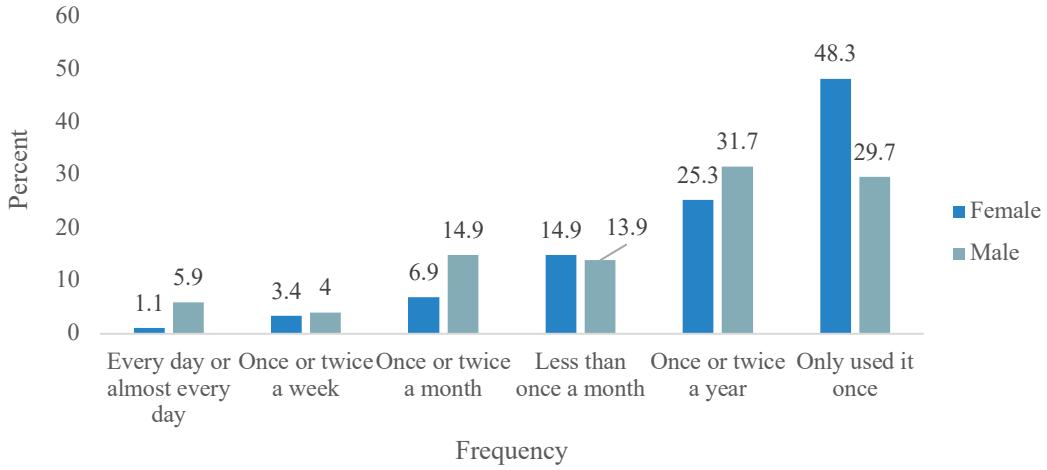
Frequency of use among those reporting lifetime cannabis use is summarized in Figure 4.4. Most participants were using cannabis infrequently, with 38.1% reporting that they had used it only once and 28.6% reported using it only once or twice a year. In contrast, 11.1% reported using once or twice a month, 3.7% were using it once or twice a week and 4.2% were using it every day or almost daily.

Figure 4.4 Frequency of Cannabis Use



Female students (48.3%) were more likely than males (29.7%) to report using cannabis only once. Five-point nine percent of males who reported cannabis use, reported using it every day or almost every day, whereas only 1.1% of females using cannabis reported this frequency of use. Figure 4.6 shows prevalence of frequency of cannabis use by gender.

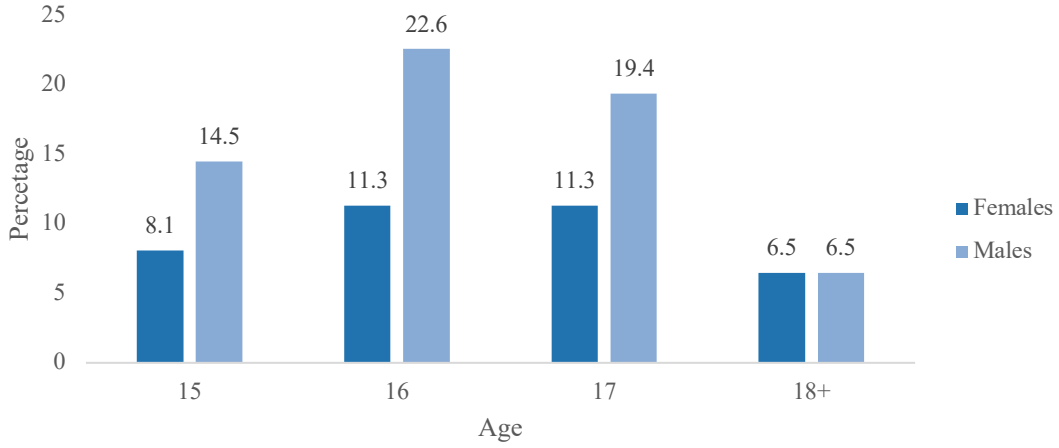
Figure 4.5 Frequency of Cannabis Use by Gender



For subsequent analyses the six level variable of frequency of cannabis use was recoded into a dichotomous variable which classified respondents as "non-frequent users" only

trying it once or using it once or twice a year (66.7% of lifetime cannabis users) or "frequent users" using cannabis at least monthly (33.3% of cannabis users). Frequent use was not significantly more prevalent among males than females (38.6% vs 26.4%; OR=.556, 95%CI=.296-1.046; p=.069) whereas results showed that frequent use was significantly more prevalent among older students than younger students (OR=.1.407, 95%CI=1.028–1.927; p=.033). The difference in the age by gender interaction was not statistically significant (OR=1.424, 95%CI=.755–2.687; p=.275).

Figure 4.6 Frequent Cannabis Use by Age and Gender



4.5.5. Frequent Cannabis Use by Ethnicity and Socioeconomic Status

Chi-square test indicated no significant differences between frequent cannabis use and ethnicity (χ^2=.649, df=3, p=.885). Frequent cannabis use was reported by 33.6% (N=37) of Hispanic or Latin lifetime cannabis users, 25% (N=3) of Caucasian, 26.7% (N=4) of participants in Other category and 30.4% (N=14) of those identifying themselves as African-Descent. In contrast, there were significant differences between frequency of cannabis use and socioeconomic status (χ^2=15.651, df=2, p=.000). Fifty two point six

percent of participants that reported ever using cannabis and that were classified as part of socioeconomic level A/B reported frequent cannabis use, 35.2% of participants classified as part of socioeconomic level C+/C/C- and 11.6% of participants classified as part of level D+/D/E reported frequent cannabis use. Results indicate that participants in the highest socioeconomic level were more likely to use cannabis frequently than participants in lower socioeconomic levels.

4.5.6. Quantity of Cannabis Used by Age and Gender

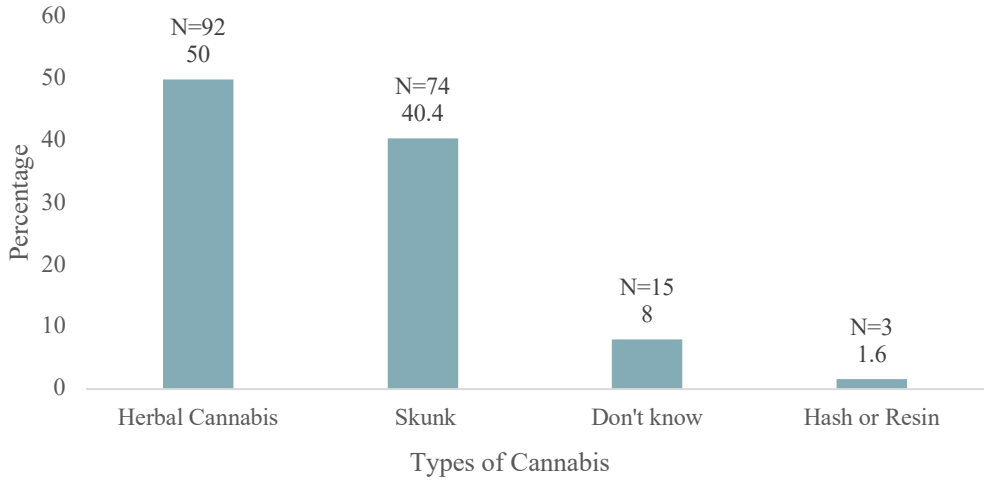
Quantity of cannabis use in the questionnaire was assessed by requesting participants to report the number of joints they use on a typical occasion. The most commonly reported quantities of use were one joint (37.3%) and ¼ of a joint (31.9%). For further analyses the original variable comprising six categories (see p. 7) was recoded into a dichotomous variable constructed as "less than one or one joint" and "two or more joints". Overall, both female and male cannabis users showed similar rates of using less than one to one joint on any typical occasion, 83.1% and 80% respectively. No significant differences were found in quantity of use by age (OR=.895, 95%CI=.596–1.342; p=.590), gender (OR=1.403, 95%CI=.617–3.192; p=.419) or by the interaction between age and gender (OR=.801, 95%CI=.352–1.820; p=.596). No significant associations were found between quantity of use and ethnicity (χ^2=1.189, df=3, p=.756) or between quantity of use and socioeconomic status (χ^2=5.690, df=2, p=.058).

4.5.7. Types of Cannabis

Students who reported lifetime cannabis use were further asked to identify the type of cannabis they mainly used, the type of cannabis that was most available to them and the one that they preferred to use. Among the 29.6% of students who reported cannabis use,

almost half (48.9%) reported herbal cannabis as the type of cannabis they mainly used (Figure 4.7). Followed by skunk, hydroponic or redhead (39.4%). Eight percent reported not knowing the type of cannabis they were using and only 1.6% reported hash as their main type of cannabis used.

Figure 4.7 Prevalence of Type of Cannabis Mainly Used



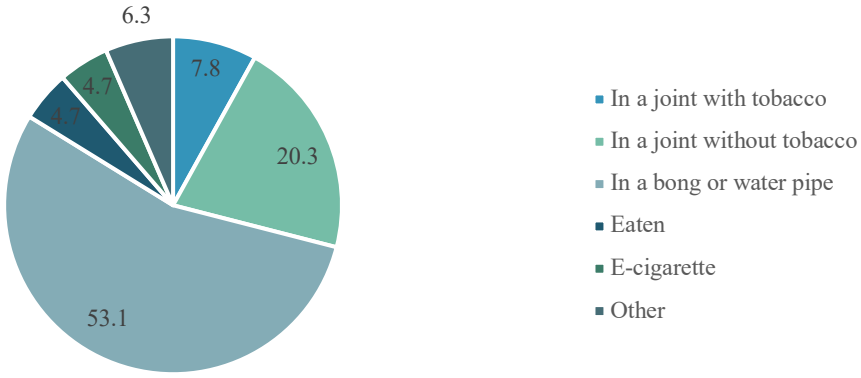
Given previous literature (Chapter 1) suggesting that the use of high potency varieties of cannabis may confer increased risk for experiencing psychotic-like experiences, it was examined whether the use of this type of cannabis varied across age, gender or other sociodemographic factors and if this variation had an impact in the appearance of psychotic-like experiences. Statistically significant differences were found in the types of cannabis mainly used when comparing high potency (skunk, hydroponic or redhead) and low potency (herbal or hash or others) cannabis use by age (OR=.700, 95%CI=.513-.956; p=.025) and by gender (OR=.438, 95%CI=.237-.810; p=.008). Results indicate that older participants were more likely to use skunk than younger participants and that males were more likely to use skunk-type cannabis than females

(22.7% vs. 12.3%). No significant differences were found between type of cannabis mainly used and the interaction by age and gender (OR=1.277, 95%CI=.680–2.400; p=.447), type of cannabis mainly used and ethnicity (χ^2=.877, df=3, p=.831) or socioeconomic status (χ^2=3.600, df=2, p=.165).

4.5.8. Routes of Administration

Regarding routes of administration or method of cannabis use, high rates of use in bong or water pipe were observed with 53.1% of students who had used cannabis reporting this as their preferred method of use. For further analyses the variable of routes of administration was recoded into a dichotomous variable categorised as bong or water pipe and any other. Odds ratios obtained from crosstabs and binary logistic regression analyses showed no significant associations in routes of administration by age (OR=1.083, 95%CI=.811–1.446; p=.590), gender (OR=.881, 95%CI=.492–1.575; p=.669) or by the interaction between age and gender (OR=1.237, 95%CI=.692–2.212; p=.473). Moreover, no statistically significant associations were found by ethnicity (χ^2=.184, df=3, p=.980) and only a marginal significance by socioeconomic level (χ^2=5.921, df=2, p=.052).

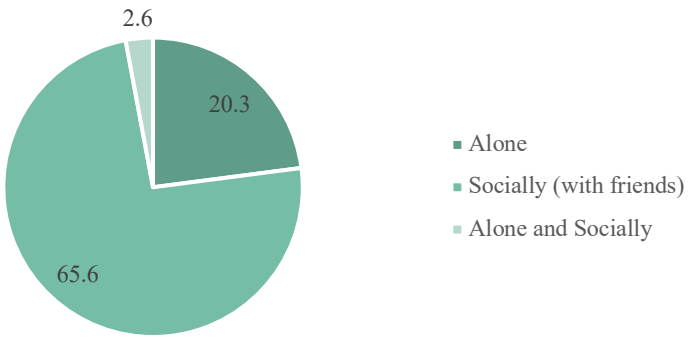
Figure 4.8 Method of Cannabis Use



4.5.9. Social and Non-Social Cannabis Use

When analysing social or non-social cannabis use, data showed that 65.6% of respondents mentioned using cannabis mainly with friends and 20.3% reported non-social cannabis use. Two-point six percent refused to select only one option, reporting that they used cannabis with the same frequency socially and non-socially.

Figure 4.9 Social or Non-Social Cannabis Use



For additional analyses the variable was recoded as a dichotomous measure considering alone or socially. Analyses showed no significant associations between social or non-

social use bye age (OR=.893, 95%CI=.626–1.275, p=.534), gender (OR=.830, 95%CI=.400–1.724; p=.618) or the interaction by age and gender (OR=1.444, 95%CI=.701–2.973; p=.319). No significant associations were found between social or non-social cannabis use and ethnicity (χ^2=6.714, df=3, p=.082) or socioeconomic status (χ^2=1.077, df=2, p=.583).

4.5.10. Cannabis Experience Questionnaire

To examine the items selected for this scale, a principal component factor analysis was conducted in which a one factor model was fitted to the data on the seven items. This analysis identified a factor with an eigenvalue of 2.73 which explained 39.07% of the total variance. The factor loadings for each of the seven items are displayed in column 4 of Table 4.1 which ranged from .552 to .694. Participants who reported lifetime cannabis use (*N=192*) completed this cannabis experience questionnaire.

Furthermore, reliability analysis of the cannabis experience questionnaire was conducted. Mean ratings for each of the seven items, the corrected item total correlation for each item and Cronbach's alpha if an item was deleted are summarised in Table 4.1. The seven-item scale had moderate to high reliability (Cronbach's Alpha = .738). All items had moderate to high item total correlations (.355 - .568) and the analysis also indicated that deleting any of the items from the scale would not improve reliability. These analyses support the use of a single scale, combining ratings across the seven items in the following analyses.

Table 4.1 Reliability Analysis: Cannabis Experience Questionnaire

Item	Mean	(SD)	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted	Factor Loadings
Feelings of paranoia or suspiciousness	1.23	.55	.397	.713	.591
Hearing voices	1.14	.46	.355	.722	.552
Feeling like I am going crazy or mad	1.17	.52	.445	.706	.637
Not wanting to do anything or lack of motivation	1.40	.70	.477	.694	.655
Difficulty in concentrating	1.58	.86	.525	.684	.665
Not able to think clearly	1.67	.86	.568	.670	.694
Seeing visions	1.35	.65	.395	.713	.568

4.5.11. Patterns of Cannabis Use, Sociodemographic Characteristics and Mean Scores of the Cannabis Experience Questionnaire

As a next stage of analyses, a series of ANOVAS were conducted to test whether self-reported mean scores in cannabis experience questionnaire differed among sociodemographic characteristics (age, gender, ethnicity, socioeconomic status) and patterns of cannabis use (age of first use of cannabis, main type of cannabis used, frequency of cannabis use and number of joints used on a typical occasion). The results of these analyses are summarised in (

Table 4.2).

These analyses indicated significantly higher mean scores on the cannabis experience questionnaire for participants who reported using cannabis frequently (defined as every day or almost daily, weekly or monthly use) compared with those who reported using the drug on only one or two occasions (F=11.543, df=1, p=.001). There was also a marginally significant difference in self-reported scores by socioeconomic status (F=3.052, df=2, p=.050); individuals from socioeconomic level C+/C/C- reported higher mean scores in the cannabis experience questionnaire (mean=9.97, SD=3.21) than those from either A/B (mean=9.19, SD=2.75) or D+/D/E (mean=8.74, SD=2.07) socioeconomic level. Analyses were conducted to understand the nature of these results and data showed that the prevalence of high quantities of cannabis use (two or more joints on any typical occasion) among participants in socioeconomic level C+/C/C- was higher (8.7%) than in participants in level A/B (5.4%) or level D+/D/E (1.6%), which explains the higher scores in the cannabis experience questionnaire.

The remaining sociodemographic characteristics and aspects of cannabis use were not significantly associated with mean scores of the questionnaire. Furthermore, linear regression analyses were conducted to identify if there were statistically significant differences between scores of the questionnaire after controlling for age of first use, age, gender and frequent or non-frequent use. Results showed that the only variable that made a significant contribution to the cannabis experience questionnaire score was frequent cannabis use (R Square=.60, F=11.875, df=1, p=.001).

Table 4.2 Cannabis Experience Questionnaire Mean Scores by Sociodemographic Characteristics and Patterns of Cannabis Use

Age (in years)	**N**	**Mean**	**SD**	**F**	**df**	**p**
15	29	10.83	3.29	2.387	3	.071
16	62	9.34	2.78			
17	53	9.43	3.16			
18-19	41	9.54	2.93			
Gender						
Female	86	9.19	2.31	2.2	(1	.140
Male	98	9.83	3.37			
Ethnicity						
Caucasian	12	9.67	2.74	.633	(3	.594
Hispanic or Latin	107	9.62	2.72			
African-Descent	45	9.62	3.61			
Other	15	9.53	2.92			
SES Level						
A/B	36	9.19	2.75	3.052	2	.050
C+/C/C-	107	9.97	3.21			
D+/D/E	42	8.74	2.07			
Age of First Use						
9 to 15	143	9.73	3.08	2.780		.097
16 to 18	42	8.88	2.28			
Main Cannabis Type						
Herbal Cannabis	90	9.22	2.35	1.580	2	.209
Skunk	71	10.03	3.46			
Hash/Mix/Don't know	20	9.35	3.07			
Frequency of Cannabis Use						
Frequent	60	10.53	3.08	11.543	1	.001*
Non-Frequent	123	9.02	2.69			
Number of Joints						
Less than 1 or 1	151	9.50	2.93	1.154	1	.284
Two or more	29	10.14	3.02			

Lifetime prevalence and frequency of use of licit and illicit drugs was assessed and data are summarized in

Table 4.3. Results showed high prevalence of the use of licit drugs, with alcohol being the most widely used among participants (80.7%), lifetime binge drinking (more than 8 units of alcohol in a single session for men, more than 6 units of alcohol in a single session for women; NHS, 2019) was reported by 64.5% of the sample. Fifty-four-point eight percent reported lifetime use of tobacco and 41.7% reported use of e-cigarettes. Regarding frequent use, alcohol was most frequently used with participants indicating using it once or twice a year (24.1%) and once or twice a month (21.6%); participants reported binge drinking once or twice a month (19.1%) and once or twice a year (18%).

Regarding tobacco and e-cigarettes, participants reported mostly infrequent use (only used it once) with 53.9% reporting e-cigarette use and 34.6% tobacco use. Mean age of first use of licit drugs was 14 years old. Regarding illicit drugs, excluding cannabis, the drug most widely used among participants was cocaine with 9.6% of participants in the whole sample reporting lifetime use of this drug; followed by hallucinogens (4.3%), solvents (4.2%) and crack (4%). Mean age of first use of the before mentioned illicit drugs was 15 years old. Regarding frequency of illicit drug use, participants mainly reported infrequent use, “only tried it once”. Forty-two point six of cocaine users reported only tried it once, hallucinogens (53.6%), solvents (85.2%) and crack (46.2%). Lastly, the least common drugs used among the school sample were heroin, opium and opioids in general (0.8%, 0.9%). Mean age of first use of any illicit drug was 14 years old.

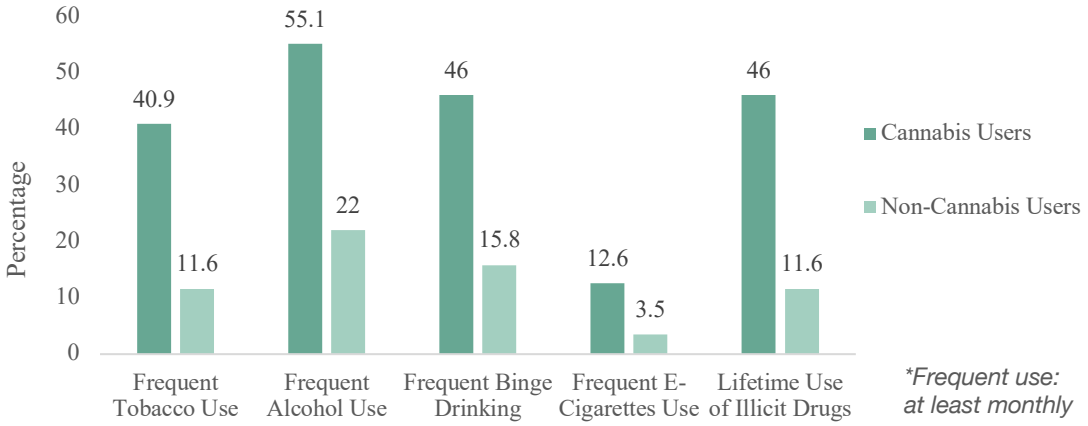
Table 4.3 Lifetime Prevalence, Age of First Use and Frequency of Use of Other Drugs

Drug	Lifetime Use (% / N)	Mean Age of First Use	Every Day Almost Daily	Once or Twice a Week	Once or Twice a Month	Less than Once a Month	Once or Twice a Year	Just Tried it Once
Tobacco	54.8/ 355	13.98	13.1	12.3	12.8	12.8	14.2	34.6
E-cigarettes	41.7/270	14.69	3.1	5.5	7.4	10.9	19.1	53.9
Alcohol	80.7/523	14	1	16.9	21.6	19.3	24.1	17
Binge Drinking	80.1/414	14	1	10.8	19.1	14.9	18	16.2
Cocaine	9.6/62	15.22	8.2	4.9	16.4	11.5	16.4	42.6
Crack	4/26	14.9	3.8	3.8	19.2	15.4	11.5	46.2
Solvents	4.2/27	14.5	0	7.4	7.4	0	0	85.2
Hallucinogens	4.3/28	15.23	3.6	3.6	10.7	10.7	17.9	53.6
Ecstasy	3.1/20	14.86	0	10	10	15	15	50
Benzodiazepines or Sleeping Pills	9/58	14.34	9.1	9.1	7.3	5.5	23.6	45.5
Opioids	0.9/6	14	0	16.7	33.3	16.7	33.3	0
Heroin or Opium	0.8/5	13.14	100	0	0	0	0	0
Amphetamines or Methamphetamines	2.9/19	14.21	100	0	0	0	0	0
Other Drugs	3.1/20	13.32	31.6	10.5	5.3	10.5	5.3	36.8

4.5.12. Frequency of Use of Other Drugs in Lifetime Cannabis Users

Frequency of use of other drugs among participants reporting cannabis use was analysed. Two categories were created; frequent use (at least monthly) and non-frequent use (only once or never).

Figure 4.10 Prevalence of Use of Other Drugs Among Cannabis Users and Non-Cannabis Users



When analysing frequency of use of other drugs (frequent vs. non-frequent) among lifetime cannabis users, results showed that 40.9% reported using tobacco frequently, 55.1% reported frequent alcohol use, 46% reported frequent binge drinking and 12.6% frequent e-cigarette use. As shown in Table 4.4 differences between frequent use of other drugs among cannabis users and non-users was noticeable.

Given the low prevalence and low frequency of use of illicit drugs a single variable of lifetime use of any illicit drug was computed by combining reports of any use of the following drugs: cocaine, crack, solvents, hallucinogens, ecstasy, benzodiazepines or sleeping pills, opioids, heroin or opium and amphetamines or methamphetamines. To

examine the associations between lifetime cannabis use and use of other drugs a series of analyses were conducted to compare rates of at least monthly or less frequent use of the licit drugs (tobacco, e-cigarettes, alcohol and binge alcohol use) and lifetime use of any illicit drug among students reporting lifetime use of cannabis. The results of these analyses are summarized in Table 4.4.

These results indicate that the use of other drugs was substantially higher in students who reported lifetime cannabis use with rates of use of these drugs being approximately 2 to 4 times higher in cannabis users than in non-cannabis users.

Table 4.4 Lifetime Cannabis Use and At Least Monthly Use of Other Drugs

At Least Monthly Use of	**Yes (%)**	**No (%)**	**OR**	**95% CI**
Tobacco	40.9	11.6	2.6	2.17-3.31
Alcohol	55.1	22	2.6	2.07-3.26
Alcohol Binge	46	15.8	2.5	2.04-3.13
E-Cigarettes	12.6	3.5	2.1	1.64-2.84
Lifetime Use of Illicit Drugs	46	11.6	3.0	2.44– 3.71

From the whole sample prevalence of lifetime cannabis use was 29.6%, cannabis use in the past six months was 14.2%. Regarding frequency of use, of the whole student sample, 19.4% reported non-frequent use of cannabis compared to 9.7% reporting frequent use.

4.6. Summary

This chapter examined patterns of cannabis use and related factors in a school sample of adolescents aged 15 to 19 years old in Mexico City and Estado de Mexico. Twenty-nine-point six percent of participants from this sample reported using cannabis at least once in their lifetime; similar to the prevalence observed in the survey conducted by Villatoro et al. in 2015, where the prevalence among high school students was of 30.1%. Moreover, results showed that prevalence of lifetime cannabis user has higher in males than in females. These results support previous surveys conducted in Mexico where prevalence of cannabis use was higher among males than females (Villatoro et al., 2015).

Regarding frequency of cannabis use analyses showed that in the overall sample, participants were more likely to report infrequent cannabis use (66.7%), particularly women, where 38.1% reported using cannabis only once. Older participants were more likely to have higher prevalence of frequent cannabis use than younger participants. Similar to these findings, international research has shown that older adolescents tend to have higher prevalence of lifetime cannabis use and higher prevalence of frequency of use (CBHSQ, 2017). Moreover, participants in higher socioeconomic levels tend to use cannabis more frequently than adolescents in lower socioeconomic levels. This might be as a result of more access to economic resources, therefore more access to obtain and use cannabis more frequently.

As previously mentioned, one of the main strengths of this study is the assessment of type of cannabis mainly used. Results indicated that of participants reporting lifetime cannabis use, 48.9% reported using herbal-type cannabis vs. 39.4% of participants

reported using skunk-type cannabis. Statistically significant differences were found when analyses were conducted among different types of cannabis and sociodemographic characteristics. Results showed that older participants were more likely to use skunk-type cannabis than younger participants and that males were more likely to use skunk-type cannabis than females. Initially, it was hypothesised that participants will report higher use of herbal cannabis and low prevalence of skunk-type cannabis. Overall, herbal cannabis use was higher than skunk, however the level of skunk use is much higher than expected. Research has shown that the use of skunk-type cannabis confers higher risk (OR=5.4, 95%CI=2.81-11.31, p=0.002) of psychotic disorders compared to other types of cannabis (Di Forti et al., 2015); therefore the importance of examining the association between type of cannabis used and psychotic-like experiences in the following chapter.

One noteworthy finding to emerge from these analyses that may be distinct to Mexico, was the high number of respondents who reported that they typically used cannabis via water pipes or bongs (53.1%). This estimate is substantially higher than that reported for the United Kingdom (Hindocha, Freeman, Ferris, Lynskey, & Winstock, 2016), where typical estimates have been in the region of 5%. Nonetheless, the current finding is consistent with previous estimates from the Global Drug Survey which reported that 47% of adult cannabis users in Mexico reported they typically used bongs or water pipes without tobacco (Hindocha et al., 2016).

Results of the assessment of use of other drugs, licit and illicit, showed high levels in lifetime prevalence of alcohol use (80.7%) and binge drinking behaviour (64.5%) followed by tobacco (54.8%) and e-cigarette use (41.7%). Mean age of first use of

alcohol, tobacco and e-cigarette use was 14 years old. Furthermore, participants reporting binge drinking, mostly reported doing it in frequent manner, with 19.1% reporting binge drinking once or twice a month. Fortnightly or monthly alcohol use was reported by 21.6% of participants and 24.1% reported using once or twice a year. The mean age of first use of any illicit drug was 14 years old. Cannabis is the primary illicit drug used by participants in the school sample (29.6%) followed by cocaine with 9.6% of prevalence of lifetime use.

Results indicate that the use of other drugs was substantially higher in students who reported lifetime cannabis use with rates of use of these drugs being approximately 2 to 4 times higher in cannabis users than in those who reported no lifetime cannabis use. Moreover, frequent use (at least monthly) of tobacco (40.9%), alcohol (55.1%) and binge drinking (46%) was particularly high among cannabis users compared with never users. Regarding illicit drugs, 46% of participants that reported lifetime cannabis use reported lifetime use of other drugs compared to 11.6% of lifetime use of illicit drugs among those who had never used cannabis; participants that reported cannabis use were almost 4 times more likely to have used illicit drugs than non-users. These findings are consistent with previous studies, conducted elsewhere, which reported strong associations between the use of cannabis and the use of other drugs (Hall, 2014; Hall & Lynskey, 2005). These findings highlight the high prevalence of cannabis use and, the high risk among cannabis users of using other illicit drugs.

5. Cannabis Use and Psychotic-Like Experiences in an Adolescent School Sample in Mexico City

5.1. Introduction

Cannabis use and its association with the appearance of psychotic-like experiences has been a subject of interest, with the first study published in 1987 (Andreasson, 1987). Research has shown there are different factors that may influence the association, for example, type of cannabis, frequency of use, adverse experiences during childhood, etc. (Bechtold et al., 2016; Morgan et al., 2014). The psychosis spectrum can range from a diagnosed clinical psychotic disorder to subclinical symptoms or experiences that may or may not disappear with time (van Os et al., 2009). Psychotic-risk symptoms include unusual thought content, suspiciousness, persecution, grandiosity, perceptual abnormalities of hallucinatory intensity and speech that is incoherent or unintelligible (McGlashan, 2001). These symptoms or experiences, when persistent can generate discomfort and lead to a more full-blown psychotic disorder later in life (Marshall & Rathbone, 2011). Similar to other psychiatric symptoms and disorders, psychotic-like experiences can be increased by other agents or circumstances e.g. trauma and family history of psychosis (Read, van Os, Morrison, & Ross, 2005), and these should be taken into account to protect individuals when at risk (Seidman et al., 2010).

There has been growing interest in whether early onset of cannabis use may be linked to a wider range of mental health problems and, in particular, psychotic-like experiences (see Chapter 1). There have been extensive debates regarding the association between cannabis and psychosis; some argue that one of the main reasons the associations between cannabis and psychosis is untrustworthy is that, prevalence of cannabis use has risen, however, the same increase in the prevalence of psychosis or schizophrenic

disorders has not been seen (Murray & Di Forti, 2016); this argument can be overturned from different perspectives. There is scarce evidence on trends of schizophrenia worldwide, and research has shown that psychotic related problems might be more complex than considered until now. Psychotic-spectrum experiences are now considered as a continuum rather than a dichotomous, present or absent diagnosis. This would make prevalence of these experiences in the general population higher than considered before (van Os et al., 2009). Moreover, research has not argued that cannabis is the main and only risk factor for the development of psychotic-like experiences, on the contrary, authors have stated that cannabis is only one of many different risk factors (Van Os, 2001) which, when combined, may increase the risk in the appearance of these symptoms (Murray & Di Forti, 2016). Furthermore, when taking into consideration that the appearance of these symptoms might only be transitory and these can change over time, then the argument of higher prevalence in cannabis use but not in the spectrum of psychotic disorders does not stand.

A consistent finding across studies is that cannabis use is associated with increased rates of psychotic-like symptoms or experiences (Barkus & Murray, 2010); and of specific interest is whether the association between cannabis use and rates of psychotic-like experiences vary according to age, with some studies suggesting that early onset of cannabis use may be associated with greater risk (Anglin et al., 2012). One of the first prospective longitudinal studies examining adolescent cannabis use as a risk factor for later diagnosis of schizophrenia while controlling for psychotic symptoms during childhood predating use of cannabis was conducted by Arsenault et al. in 2002. Results showed that participants who used cannabis by age 15 had higher risk (OR=4.65, 95%CI=1.84–11.78) of having a diagnosis of schizophrenia by age 26 (Arseneault et al.,

2002), however one important limitation of that study was the small sample size in the <15 age group, with only 29 participants included in that group.

Furthermore, a review conducted in 2015, where seventeen papers met the inclusion criteria, examining the relationship between adolescent onset of regular cannabis use and the onset of prodromal symptoms, concluded that the appearance of psychotic like experiences is associated with early onset and regular use of cannabis, particularly in participants at greater risk for developing psychotic disorders (Bagot et al., 2015). However, there is an important difficulty to be mention between age of onset of cannabis use and duration of use. Age of onset of cannabis use refers to the first-time participants tried cannabis; however, this differs significantly to the age of onset of regular cannabis use. This difference is important as research has shown, as stated below, that continuous use increases the risk of psychotic-like experiences. A meta-analysis examining the association between level of cannabis use and risk for psychosis in participants without history of mental health problems (Marconi et al., 2016) identified a pooled estimate reported as the increased risk in the development of psychosis relative to a continuous level of cannabis exposure showing that cannabis users with higher frequency of use were 3.9 times at more risk of developing psychotic disorders or psychotic-like symptoms than non-users (unadjusted OR=3.9; 95%CI=2.84–5.34).

In addition, in 2014 a study explored the relationship between early onset of cannabis use, frequency of use, type of cannabis being used (high-potency / low-potency) and the age of onset of psychosis in a first episode psychosis sample (Di Forti et al., 2014). Researchers found that participants who started using cannabis by age 15 or younger

had an earlier age of onset of psychosis (m=27, SD=6.2; median=26.9) than those who started use after 15 (mean=29.1, SD=8.5; median=27.8) (HR=1.40; 95%CI=1.06 – 1.84; p=.050). Moreover, among all groups, daily users of high-potency cannabis had the earliest age of onset of psychosis (mean=25.2, SD=6.3; median=24.6) compared to non-users (HR=1.99; 95%CI=1.50 – 2.65; p<.0001).

To the best of my knowledge, research regarding cannabis use and psychotic-like experiences has not been conducted in Mexico, although cannabis use among adolescents has been increasing during the last decade (see Chapter 1). Therefore, the present study examines different patterns of cannabis use and its association with psychotic-like experiences.

5.2. Objectives

- To evaluate the psychometric properties of the PRIME Screen Questionnaire used to identify prevalence and extent of psychotic-like experiences.
- To estimate the prevalence of psychotic-like experiences among 15 to 19-year-old students in Mexico City.
- To examine potential associations between patterns of cannabis use, type of cannabis mainly used and psychotic-like experiences.
- Identify if cannabis use predicts presence of psychotic-like experiences.
- Identify if high quantity of cannabis use predicts presence of psychotic-like experiences.
- Identify if high frequency of cannabis use predicts presence of psychotic-like experiences.

- Identify if high scores in a combined quantity by frequency measure of cannabis predicts the presence of psychotic-like experiences.

5.3. Statistical Analysis

Analyses were conducted using the statistical package IBM SPSS Statistics Version 25, Release 25.0.0.1 64-bit edition.

5.3.1. Prevalence of Psychotic-Like Experiences

Firstly, mean scores of each item of the psychotic-like experiences assessment were analysed by gender to identify how prevalent each symptom was, and specifically identify if there were any differences by gender. Descriptive statistics were conducted to identify the prevalence of psychotic-like experiences by age and gender in the school sample. Subsequently, principal component factor analysis and reliability analysis were conducted to the PRIME Screen Questionnaire.

5.3.2. Cannabis Use and Psychotic-Like Experiences', Sociodemographic Characteristics and Use of Other Drugs

Analyses of variance were conducted to identify the associations between cannabis use with sociodemographic characteristics and the use of other drugs. For these analyses a continuous variable of cannabis use was created by multiplying scores of two variables, quantity by frequency of cannabis use. Moreover, to identify associations between psychotic-like experiences with sociodemographic factors and use of other drugs same analyses were conducted. The continuous variable from the PRIME Screen

questionnaire employed for the analyses was the total score of the thirteen items in the questionnaire.

A number of different dichotomous measures of cannabis use (lifetime use, at least monthly use and type of cannabis mainly used) were employed and some created to explore the associations these may have with sociodemographic characteristics and use of other drugs. Lifetime cannabis use was explored as one question and, in the analyses, this question remained the same. The at least monthly variable was created from the original question of frequency of use, which initially had 6 categories and was modified to only a two-category variable: at least monthly use and sometimes or never. Lastly, the variable of type of cannabis mainly used was modified to only consider non-users, skunk type of cannabis and any other type of cannabis used. Once these variables were created, odds ratios obtained from crosstabs, chi-square and logistic regression analyses were conducted.

5.3.3. Associations between Psychotic-Like Experiences, Sociodemographic Characteristics and Use of Other Drugs

For the psychotic-like experiences analyses, a dichotomous measure was created. As previous literature showed (Kobayashi, H. et al., 2008) it was feasible to create a positive/negative outcome of presence or absence of psychotic-like experiences using the PRIME Screen Questionnaire. In the questionnaire used for the present study, a 40+ score in the psychotic-like experiences assessment would result in having a positive score. Once this variable was created, odds ratio obtained from crosstabs, chi-square and logistic regression analyses were conducted to identify associations between a

positive score in the PRIME Screen Questionnaire, sociodemographic characteristics and use of other drugs.

5.3.4. Cannabis Use, Psychotic-Like Experiences, Sociodemographic Characteristics and Use of Other Drugs: Regression Models

Following these analyses, independent regression models were structured. Firstly, with each of the different measures of cannabis use, sociodemographic characteristics and use of other drugs. These analyses were conducted to see how sociodemographic factors and use of other drugs interacted with cannabis use once all variables were included in one model. Then, the same model was applied for the psychotic-like experiences assessment to identify the associations while controlling for all the before mentioned variables.

5.3.5. Associations between Cannabis Use and Psychotic-Like Experiences

Preliminary analyses to identify associations between psychotic-like experiences and different measures of cannabis use were conducted. These analyses comprised of odds ratio obtained from crosstabs, using the dichotomous measure of the PRIME, lifetime cannabis use and at least monthly cannabis use. For the three-category variable of type of cannabis mainly used (non-users, skunk, any other type of cannabis), chi-square analyses were conducted.

5.3.6. Association between Cannabis Use and Psychotic-Like Experiences while Controlling for Sociodemographic Characteristics and Use of Other Drugs

To examine the associations between different measures of cannabis use and psychotic-like experiences while controlling for sociodemographic characteristics and use of other drugs multiple regression analyses were conducted. Linear regression analyses were conducted for the continuous measure of the cannabis use (QFS) and the total score of the PRIME Screen questionnaire. Logistic regression analyses were run for the dichotomous measures of cannabis use and psychotic-like experiences, and multinomial logistic regression analyses were conducted for the type of cannabis mainly used, which included three different categories. Furthermore, multilinear regression analyses were conducted to identify differences among scales of quantity by frequency scales of cannabis use of the different types of cannabis. These analyses are the core and main interest of the present study.

5.4. Results

5.4.1. Psychotic-Like Experiences Assessment: The PRIME Screen Questionnaire

As previously mentioned, the questionnaire employed for the assessment of psychotic-like experiences was the PRIME Screen Questionnaire. Analyses were conducted to obtain mean scores of each item according to gender, to identify differences and similarities between females and males. These analyses were conducted to acknowledge how participants responded, to comprehend how prevalent each symptom was, and to identify if there were statistically significant differences in responses by gender (Table 5.1). The item with highest mean scores was exploring the presence of odd or unusual experiences (females=2.88; males=2.61), followed by the ability to discern if what its being experienced is real, just a product of their imagination or a dream (females=2.73; males=2.56). Concern regarding people planning to hurt them or about to hurt them was also one of the items with higher scores among participants (females=2.70; males=2.48). Overall, it was observed that females obtained higher mean scores than males, and to identify if differences were statistically significant, analyses of variance were conducted on each item by gender. Results show significant differences in two items. Firstly, the item related to predicting the future ($F=4.29$; $df=1,640$; $p=.039$) and, on the item related to hearing faint or clear sounds of people talking when no one is around ($F=4.643$; $df=1, 639$; $p=.032$).

Table 5.1 Item Analysis on Mean Scores by Gender: PRIME Screen Questionnaire

Item	Mean		F	df^1, df^2	p
	Females	Males			
Odd or unusual things I can't explain	2.88	2.61	3.171	1, 641	.075
I might be able to predict the future	1.80	2.05	4.29	1, 641	.039*
Something interrupting or controlling my thoughts, feelings or actions	2.38	2.13	3.204	1, 641	.074
Changed my behaviour because of my superstitions	2.24	2.08	1.339	1, 639	.248
Confusion about experiences being real, part of my imagination or dreams	2.73	2.56	1.173	1, 638	.279
Others can read my mind, or I can read other's minds	1.36	1.34	.079	1, 640	.778
I wonder if people are planning to hurt me or about to hurt me	2.70	2.48	2.119	1, 637	.146
I have special natural or supernatural gifts	1.25	1.35	1.688	1, 640	.194
My mind might be playing tricks on me	2.18	2.16	.025	1, 639	.874
Faint or clear sounds of people talking when no one is around	2.43	2.11	4.643	1, 639	.032*
I may hear my own thoughts said out loud	2.52	2.29	2.286	1, 637	.131
I might be going crazy	1.56	1.54	.059	1, 636	.808
Visual hallucinations	2.12	1.87	3.291	1, 640	.070

5.4.2. Factor Analysis

For further exploration of the psychotic-like experiences assessment, factor analysis was conducted on the PRIME Screen questionnaire. Prior to performing the analysis, the suitability of data for factor analysis was assessed. Principal components analysis revealed the presence of 2 components with eigenvalues exceeding 1, explaining 38.1% and 8.6% of the variance respectively (Table 5.2).

Table 5.2 Total Variance of Factor Analysis PRIME Screen Questionnaire

	Initial Eigenvalues			Rotation Sums of Squared Loadings
Component	**Total**	**% of Variance**	**Cumulative %**	**Total**
1	4.915	37.809	38.809	4.687
2	1.109	8.528	46.337	2.841

The two factors obtained from preliminary analysis explain a total of 46% of the variance. All items loaded strongly on the first factor (above .4), and five components out of thirteen loaded positively in both factors. Three of them having a higher load in factor number one (above .6) and two having a higher load on factor number two. However, loadings in factor one is strong (above .4), which suggest that one-factor solution can be appropriate (Table 5.3).

As a strong correlation between the two components was shown (.473) and an inspection of the screeplot revealed a clear break from the second component onwards (the suggestion is to retain only the factors above the elbow as these factors contribute the most to the explanation of the variance) using Catell's screeplot test it was decided to retain one component for further investigation.

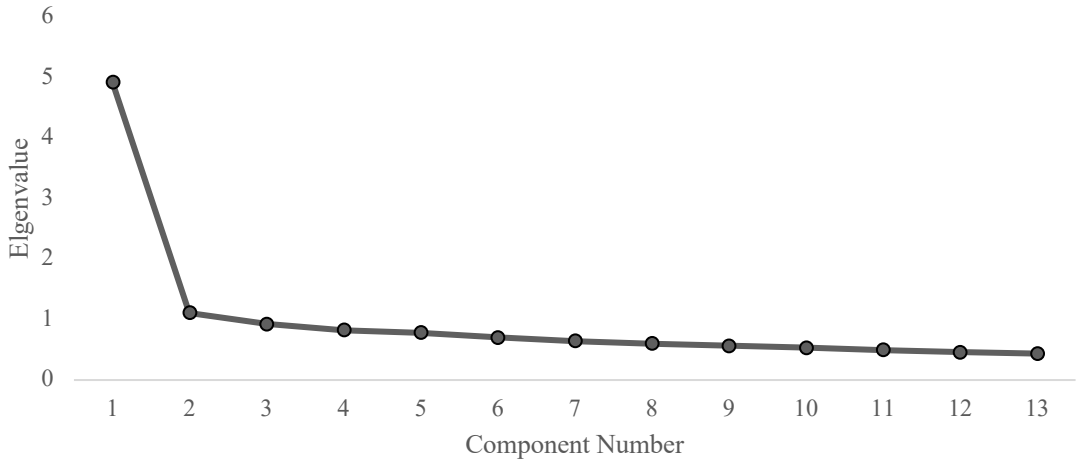
Table 5.3 Principal Components Analysis: PRIME Screen Questionnaire

Items	1	2
My mind might be playing tricks on me	.743	-.093
Confusion about experiences being real, part of my imagination or dreams	.707	-.227
Something interrupting or controlling my thoughts, feelings or actions	.636	-.096
I wonder if people are planning to hurt me or about to hurt me	.649	-.179
Visual hallucinations	.654	-.104
Changed my behaviour because of my superstitions	.632	.005*
I may hear my own thoughts said out loud	.632	-.169
Odd or unusual things that I can't explain	.596	-.181
Faint or clear sounds of people talking when no one is around	.612	-.282
I might be going crazy	.580	.153*
I might be able to predict the future	.526	.412*
Others can read my mind, or I can read other's minds	.504	.547*
I have special natural or supernatural gifts	.461	.602*

Extraction Method: Principal Component Analysis (2 components extracted)

The one-component solution explained a total of 38.1% of the variance. Moreover, general magnitude of factor loadings obtained from a principal component analysis ranged from .478 to .743 indicating all items load strongly in this component and are shown in Table 5.3.

Figure 5.1 Factor Analysis Screeplot PRIME Screen Questionnaire



In addition, reliability analysis of the PRIME Screen questionnaire was conducted. The twelve-item scale plus the extra item added to assess visual hallucinations, had high reliability (Cronbach's Alpha = .860). Regarding the exploration of Cronbach's Alpha, if any of the items was deleted, results indicated that the total alpha would not increase if any of the items were deleted. Moreover, the values obtained for the corrected item-total correlation indicate all items are correlated and evaluate the same construct (.374 - .663). This evidence supports the use of a continuous measure of psychotic-like experiences for further analysis and the one-component solution for the PRIME Screen Questionnaire.

Table 5.4 Reliability Analysis PRIME Screen Questionnaire and Principal Component Analysis

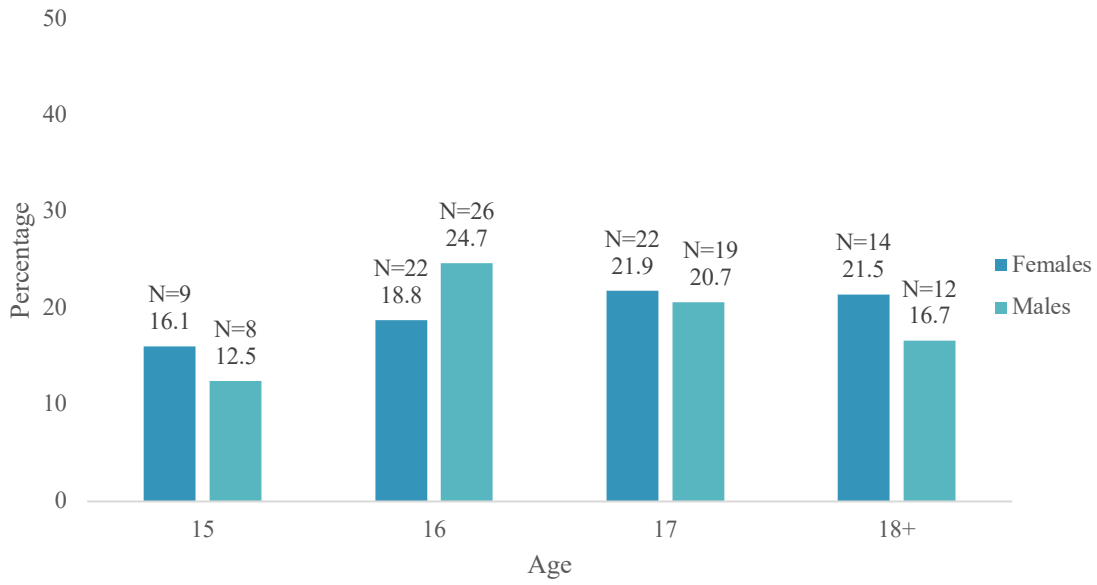
	Reliability Analysis		PCA*
Item	**Corrected Item-Total Correlation**	**Cronbach's Alpha if Item Deleted**	**Component 1**
Odd or unusual things I can't explain	.514	.851	.596
I might be able to predict the future	.436	.855	.526
Something interrupting or controlling my thoughts, feelings or actions	.549	.849	.636
Changed my behaviour because of my superstitions	.547	.849	.632
Confusion about experiences being real, part of my imagination or dreams	.629	.843	.707
Others can read my mind, or I can read other's minds	.415	.857	.504
I wonder if people are planning to hurt me or about to hurt me	.564	.848	.649
I have special natural or supernatural gifts	.374	.859	.461
My mind might be playing tricks on me	.663	.841	.743
Faint or clear sounds of people talking when no one is around	.527	.850	.612
I may hear my own thoughts said out loud	.543	.849	.632
I might be going crazy	.489	.853	.580
Visual hallucinations	.568	.848	.654

**Principal Component Analysis*

5.4.3. Prevalence of Psychotic-Like Experiences

Using a cut-off from 40+ rating points or more on the PRIME Screen questionnaire described, 20.4% of the sample were classified as positive in presence of psychotic-like experiences. Figure 5.2 shows the prevalence of these experiences by age and gender. These analyses were conducted for the only purpose of examining the data and observe differences according to gender and age. Furthermore, research has shown that psychotic-like experiences, in some groups, tend to increase during early adolescence and decline over time (Mackie et al., 2013).

Figure 5.2 Prevalence of Psychotic-Like Experiences by Age and Gender



5.4.4. Cannabis Use and Psychotic-Like Experiences', Sociodemographic Characteristics and Use of Other Drugs

To further explore the extent to which cannabis use and psychotic-like experiences have similar associations with sociodemographic characteristics and use of other drugs, licit and illicit, further analyses were conducted. The continuous variable of the PRIME Screen Questionnaire, which was obtained by adding the scores of all the items in the questionnaire provided by participants and the continuous measure of cannabis use, obtained by multiplying quantity of use (number of joints or number of grams) by frequency of use, were employed. Afterwards, the variable was log transformed to account for the non-normal distribution of the variable.

5.4.5. Mean Differences in Psychotic-Like Experiences by Sociodemographic Characteristics and Use of Other Drugs

Regarding the psychotic-like experience assessment, as shown in Table 5.5, no significant differences were found in the mean scores of the PRIME scale by age ($F=1.54$, $df=3, 639$; $p=.204$), gender ($F=2.37$, $df=1, 639$; $p=.124$) or socioeconomic status ($F=.404$ $df=2, 640$; $p=.668$). On the other hand, significant differences were found in total scores of the psychotic-like experiences questionnaire and ethnicity ($F=1.97$, $df=3, 629$; $p=.031$), with higher mean scores in the PRIME among participants identifying themselves as 'Other'. Furthermore, lifetime tobacco users had higher mean scores in the PRIME Screen Questionnaire than never users ($F=15.05$, $df=1, 636$; $p=.000$). Similarly, lifetime e-cigarette users ($F=7.64$, $df=1, 628$; $p=.006$), lifetime alcohol users ($F=8.12$, $df=1, 638$; $p=.005$) and lifetime use of any illicit drug ($F=13.35$, $df=1, 635$; $p=.000$) had higher mean scores on the psychotic-like experiences questionnaire (Table 5.5).

5.4.6. Mean Differences between Cannabis Use, Sociodemographic Characteristics and Use of Other Drugs

Analyses were conducted to identify differences and associations between different patterns of cannabis use (QFSA), sociodemographic characteristics and use of other drugs (Table 5.5). For the quantity by frequency scale (QFSA) results showed significant differences by gender in mean scores ($F=4.17$, $df=1, 643$; $p=.042$) with mean scores of cannabis use being higher among males (.33) than females (.25). No differences were shown in mean scores of the cannabis use scale by age ($F=.65$, $df=3, 644$; $p=.585$), ethnicity ($F=.34$, $df=3, 631$; $p=.800$) or socioeconomic status ($F=1.46$, $df=2, 645$; $p=.234$). There were statistically significant differences in mean scores of the QFSA and the use of tobacco ($F=91.80$, $df=1, 641$; $p=.000$), e-cigarettes ($F=50.47$, $df=1, 632$; $p=.000$), alcohol ($F=26.68$, $df=1, 644$; $p=.000$), binge drinking ($F=9.91$, $df=1, 526$; $p=.001$) and use of any illicit drug ($F=106.57$, $df=1, 623$; $p=.000$). Across all these comparisons, mean levels of the quantity by frequency scale of cannabis use were higher among those who reported using other drugs (Table 5.5).

Table 5.5 Differences in Mean Scores of the Quantity by Frequency Scale, Mean Scores of the Psychotic-Like Experiences, Sociodemographic Characteristics and Use of Other Drugs

		PRIME (M)	F	df^1, df^2	p	*QFS (M)	F	df^1, df^2	p
Age	15	25.66	1.54	3, 639	.204	.24	.647	3, 644	.585
	16	28.52				.29			
	17	27.77				.29			
	18-19	26.21				.32			
Gender	Female	28.11	2.37	1, 639	.124	.25	4.17	1, 643	.042*
	Male	26.47				.33			
Ethnicity	Caucasian	23.19	1.97	3, 629	.031*	.29	.34	3, 631	.800
	Hispanic / Latin	28.19				.28			
	African-Descent	25.86				.28			
	Other	29.68				.36			
SES	A/B	26.75	.404	2, 640	.668	.36	1.46	2, 645	.234
	C+/C/C-	27.18				.27			
	D+/D/E	28.18				.29			
Tobacco	Yes	29.21	15.05	1, 636	.000*	.44	91.80	1, 641	.000*
	No	25.10				.10			
E-cigarette	Yes	28.94	7.64	1, 628	.006*	.44	50.47	1, 632	.000*
	No	25.98				.18			
Alcohol	Yes	28.09	8.12	1, 639	.005*	.34	26.68	1, 644	.000*
	No	24.28				.10			
Binge Drinking	Yes	27.94	1.72	1, 632	.190	.38	9.91	1, 526	.002*
	No	26.47				.21			
Other Drugs	Yes	30.68	12.35	1, 635	.000*	.61	106.57	1, 623	.000*
	No	26.32				.19			

**QFS: Quantity by frequency scale*

5.4.7. Associations between Cannabis Use, Sociodemographic Characteristics and Use of Other Drugs

Analyses were conducted to identify associations between different patterns of cannabis use (lifetime cannabis use, at least monthly cannabis use, type of cannabis mainly used) and sociodemographic characteristics. Results are shown in Table 5.6. No significant differences were found between lifetime cannabis use and age (OR=1.12, 95%CI=.95-1.33; p=.183) or age by gender interaction (OR=.86, 95%CI=.61-1.22; p=.401). Furthermore, no statistically significant differences were found in the chi-square analyses of lifetime cannabis use by ethnicity (X^2=2.39, df=3, 631; p=.495) or socioeconomic status (X^2=4.17, df=2, 644; p=.125). Significant differences were found in lifetime cannabis use by gender (OR=1.44, 95%CI=1.03-2.03), indicating that males were more likely to report lifetime cannabis use than females.

Furthermore, analyses conducted to estimate associations between use of other drugs and lifetime cannabis use indicated that lifetime cannabis users were 6 times more likely to report lifetime tobacco use (OR=6.59, 95%CI=4.32-10.06) and 3 times more likely to have ever used e-cigarettes (OR=3.23, 95%CI=2.26-4.60). Furthermore, participants reporting lifetime cannabis use were four times more likely to have used alcohol (OR=4.90, 95%CI=2.63-9.13) and two times more likely to report lifetime binge drinking (OR=2.70, 95%CI=1.61-4.52). Moreover, participants that reported lifetime cannabis use were six time more likely to report use of any other illicit drug than never cannabis users (OR=6.85, 95%CI=4.59-10.23). Results are described in Table 5.6.

Table 5.6 Associations between Cannabis Use, Sociodemographic Characteristics and Use of Other Drugs: Logistic Regression, Odds Ratios and Chi-Square Analysis

		Lifetime				Monthly				Type of Cannabis			
		%	**OR**	**95%CI**	**p**	**%**	**OR**	**95%CI**	**p**	**%**	**X^2**	**df**	**p**
Age	15	26.1	1.12	.95-1.33	.183	7.6	.933	.661-1.32	.691	6.7	6.83	6	.337
	16	29.8				4.6				11			
	17	29.6				5.9				14			
	18-19	33.9				5				16.3			
Gender	Female	26.3	1.44	1.03-2.03	.035*	3	2.94	1.39-6.23	.005*	8	10.75	2	.005*
	Male	33.8				8.3				16.3			
		%	**X^2**	**df**	**p**	**%**	**X^2**	**df**	**p**	**%**	**X^2**	**df**	**p**
Ethnicity	Caucasian	33.3	2.39	3	.495	2.5	1.17	3	.759	9.5	3.93	6	.687
	Hispanic / Latin	28.6				5.2				11.8			
	African-Descent	28.2				5.5				12.2			
	Other	39.5				7.9				15.4			
SES	A/B	37.9	4.166	2	.125	10.8	8.45	2	.015*	13.5	10.42	4	.034*
	C+/C/C-	27.6				5.5				12.9			
	D+/D/E	30.3				2.1				8.5			
		%	**OR**	**95%CI**	**p**	**%**	**OR**	**95%CI**	**p**	**%**	**X^2**	**df**	**p**
Tobacco	Yes	45.2	6.59	4.32-10.06*	-	9.1	7.15	2.50-20.45*	-	18	81.72	2	.000*
	No	11.1				1.4				4.9			
E-cigarette	Yes	43.7	3.23	2.26-4.60*	-	10	4.92	2.20-11.02*	-	17	47.25	2	.000*
	No	19.4				2.2				8.2			
Alcohol	Yes	34.6	4.90	2.63-9.13*	-	6.4	2.72	.821-9.02	-	14	27.56	2	.000*
	No	9.8				2.4				4.1			
Binge Drinking	Yes	39.2	2.70	1.61-4.52*	-	7.5	4.33	1.02-18.39*	-	16.7	47.73	2	.000*
	No	19.3				1.8				3.9			
Other Drugs	Yes	62	6.85	4.59-10.23*	-	16.9	10.48	4.77-23.03*	-	32.5	111.75	2	.000*
	No	19.2				1.9				5.8			

Significant differences were found between males and females in the prevalence of monthly cannabis use, which was higher among males than females (OR=2.94, 95%CI=1.39-6.23; p=.005). Additionally, chi-square analyses showed significant associations between socioeconomic status (X^2=8.45, df=2, 642; p=.015), and monthly cannabis use, being higher in socioeconomic status A/B than in socioeconomic status C+/C/C or D+/D/E. Among participants reporting monthly cannabis use, prevalence was higher in the use of other drugs, compared to experimental users or non-users. Significant associations were found with lifetime tobacco use (OR=7.15, 95%CI=2.50-20.45), e-cigarette use (OR=4.92, 95%CI=2.20-11.02), binge drinking (OR= 4.33, 95%CI=1.02-18.39) and use of any illicit drug (OR=10.48, 95%CI=4.77-23.03), meaning that monthly cannabis users were more likely to have ever used tobacco, e-cigarettes, binge drink and any illicit drugs (Table 5.6).

Lastly, chi-square analyses showed significant associations between type of cannabis mainly used and gender (X^2=10.75, df=2, p=.005), indicating males were more likely to use skunk type cannabis than females. Furthermore, participants in socioeconomic level A/B had significantly higher prevalence of skunk use than participants in any other socioeconomic levels (X^2=10.42, df=4, p=.034) Furthermore, participants using skunk-type cannabis had higher prevalence of lifetime tobacco (X^2=81.72, df=2, p=.000), e-cigarette (X^2=47.25, df=2, p=.000), alcohol (X^2=27.56, df=2, p=.000), binge drinking (X^2=47.73, df=2, p=.000) and use of other illicit drugs (X^2=111.75, df=2, p=.000) than participants using herbal-type cannabis (Table 5.6).

5.4.8. Associations between Psychotic-Like Experiences, Sociodemographic Characteristics and Use of Other Drugs

Logistic regression, chi-square and odds ratios obtained through crosstab analyses were conducted to examine the associations between psychotic-like experiences, sociodemographic characteristics and lifetime use of other drugs (Table 5.7). A positive score in the psychotic-like experiences questionnaire was obtained with a score of 40+. Logistic regression analyses indicated no significant differences between psychotic-like experiences by age or gender. Significant associations were found by ethnicity (X^2=8.21, df=3, 630; p=.042), with participants identified as 'Other' type of ethnicity obtaining higher mean scores in the PRIME Screen Questionnaire.

Furthermore, chi-square analyses showed no association between psychotic-like experiences and socioeconomic status (X^2=.615, df=2, 643; p=.735). Regarding use of other drugs, participants reporting lifetime tobacco use (OR=1.66, 95%CI=1.10-2.50) and e-cigarettes (OR=1.50, 95%CI=1.01-2.24) were more likely to have a positive score in the psychotic-like experiences assessment. Moreover, participants reporting use of any illicit drug were two times more likely (OR=2.01, 95%CI=1.32-3.08) to score positively in the PRIME. Overall, results indicated that participants reporting lifetime use of e-cigarettes and lifetime use of any illicit drugs were more likely to have higher mean scores in both, the quantity by frequency scale of any type of cannabis and the psychotic-like experiences assessment.

Table 5.7 Associations between Psychotic-Like Experiences, Sociodemographic Characteristics and Use of Other Drugs: Logistic Regression, Odds Ration and Chi-Square Analysis

		PLE's (%)	OR	95%CI	p
Age	15	15.1	1.07	.88-1.31	.477
	16	20.7			
	17	21.1			
	18-19	18.9			
Gender	Female	19.5	1.00	.68-1.48	1.00
	Male	19.5			
		%	**X^2**	**df**	**p**
Ethnicity	Caucasian	14.3	8.21	3, 630	.042*
	Hispanic or Latin	20.3			
	African-Descent	15			
	Other	34.2			
SES	A/B	20.6	.615	2, 643	.735
	C/C+/C-	18.5			
	D+/D/E	21.3			
		%	**OR**	**95%CI**	
Tobacco	Yes	23.1	1.66	1.10-2.50*	-
	No	15.3			
E-cigarette	Yes	22.7	1.50	1.01-2.24*	-
	No	16.3			
Alcohol	Yes	20.8	1.64	.94-2.86	-
	No	13.8			
Binge Drinking	Yes	20.1	1.07	.71-1.62	-
	No	19			
Other Drugs	Yes	28.7	2.01	1.32-3.08*	-
	No	16.6			

5.4.9. Association between Different Measures of Cannabis Use by Sociodemographic Characteristics and Use of Other Drugs: Regression Models

To estimate associations between cannabis use, sociodemographic characteristics and use of other drugs regression analyses were conducted. Linear regression was conducted with the continuous measures of cannabis (QFSA). Logistic regression analyses were conducted with the dichotomous measures of cannabis use: lifetime cannabis use, at least monthly cannabis use; and for type of cannabis (3 category variable) multinomial regression analyses were conducted.

To estimate associations between psychotic-like experiences, sociodemographic characteristics and use of other drugs, linear regression analysis was conducted with the continuous measure of the PRIME Screen Questionnaire. All models included nine independent variables: age, gender, ethnicity, socioeconomic status, lifetime tobacco use, lifetime e-cigarette use, lifetime alcohol use, binge drinking, and lifetime use of any illicit drugs.

Table 5.8 Association between Patterns of Cannabis Use, Sociodemographic Characteristics and Use of Other Drugs: Regression Models

	QFSA			Lifetime Use			Monthly Use			Skunk-Type vs Non-Users			Skunk-Type vs. Herbal		
	B	**SE**	**p**	**OR**	**95%CI**	**p**	**OR**	**95%CI**	**p**	**OR**	**95%CI**	**p**	**OR**	**95%CI**	**P**
Age	.000	.02	.993	.97	.79-1.20	.760	.73	.48-1.10	.132	.88	.65-1.19	.406	.78	.56-1.09	.145
Gender	.056	.04	.113	1.52	1.00-2.29	.048*	2.92	1.22-7.02	.017*	2.51	1.39-4.56	.002*	2.70	.40-5.23	.003*
Ethnicity	.022	.03	.377	1.14	.85-1.52	.378	1.33	.77-2.29	.308	1.85	.38-9.04	.447	1.72	.33-8.92	.520
SES	-.010	.03	.737	.95	.68-1.32	.751	.48	.26-.89	.020*	.64	.25-1.68	.367	.72	.26-1.99	.522
Tobacco	.189	.04	.000*	3.40	2.07-5.56	.000*	3.30	.93-11.68	.064	2.65	1.28-5.47	.008*	.80	.33-1.92	.618
E-cigarette	.096	.04	.012*	1.56	1.02-2.39	.039*	2.98	1.09-8.16	.034*	1.41	.78-2.56	.262	.70	.35-1.39	.305
Alcohol	-.032	.06	.591	.87	.36-2.10	.758	.20	.03-1.49	.116	.35	.08-1.53	.161	.31	.06-1.72	.180
Binge Drinking	.105	.05	.030*	2.36	1.27-4.40	.006*	3.36	.72-15.67	.123	5.55	1.82-16.96	.003*	3.18	.95-10.65	.061
Other Drugs	.318	.04	.000*	4.45	2.87-6.90	.000*	7.78	3.20-18.82	.000*	8.08	4.45-14.66	.000*	2.71	1.41-5.22	.003*

Significant associations were found when conducting linear regression analyses between the quantity by frequency scale of cannabis use, sociodemographic characteristics and use of other drugs while controlling for confounding factors with lifetime tobacco use (B=.189, SE=.04, p=.000); lifetime use of e-cigarettes (B=.096, SE=.04, p=.012), lifetime history of binge drinking (B=.105, SE=.05, p=.030) and lifetime illicit drug use (B=.318, SE=.04, p=.000). Results are summarised in Table 5.8. Participants reporting lifetime use of cannabis were more likely to binge drink, use tobacco, e-cigarettes and other illicit drugs than never cannabis users. The logistic regression model estimated significant associations between lifetime cannabis use and gender (OR=1.52, 95%CI=1.00-2.29, p=.048), tobacco (OR=3.40, 95%CI=2.07-5.56, p=.000), e-cigarette (OR=1.56, 95%CI=1.02-2.39, p=.039), binge drinking (OR=2.36, 95%CI=1.27-4.40), p=.006) and illicit drugs (OR=4.45, 95%CI=2.87-6.90, p=.000) after controlling for all confounding variables (Table 5.8).

Additionally, at least monthly cannabis use was associated with gender (OR=2.92, 95%CI=1.22-7.02, p=.017), socioeconomic status (OR=.48, 95%CI=.26-.89, p=.020), lifetime use of e-cigarettes (OR=2.98, 95%CI=1.09-8.16, p=.034) and lifetime use of any illicit drug (OR=7.78, 95%CI=3.20-18.82, p=.000). Males were two times more likely than women to report at least monthly cannabis use. Participants in higher socioeconomic status had higher prevalence of monthly cannabis use than participants from lower socioeconomic status. Furthermore, monthly users were two times more likely to report e-cigarette use and seven times more likely to have experimented with any illicit drug in their lifetime. Multinomial logistic regression analyses were conducted to identify associations between the three-category variable of different types of cannabis mainly used, sociodemographic factors and use of other drugs. Significant

associations were found between participants using skunk and gender (OR=2.51, 95%CI=1.39-4.56, p=.002), tobacco (OR=2.65, 95%CI=1.28-5.47, p=.008), binge drinking (OR=5.55, 95%CI=1.82-16.96, p=.003) and other drugs (OR=8.08, 95%CI=4.45-14.66, p=.000) compared with non-users. Furthermore, when examining associations between skunk type cannabis users vs. users of any other type of cannabis, analyses showed significant associations between skunk users with gender (OR=2.70, 95%CI=1.40-5.23, p=.003) and use of any illicit drugs (OR=2.71, 95%CI=1.41-5.22, p=.003) (Table 5.8).

Table 5.9 Association between Measures of Psychotic-Like Experiences, Sociodemographic Characteristics and Use of Other Drugs: Linear Regression Models

	Total Score PRIME		
	B	**SE**	**p**
Age	-.284	.554	.609
Gender	-1.786	1.108	.108
Ethnicity	.389	.781	.618
SES	.466	.899	.604
Tobacco	2.595	1.269	.041*
E-cigarette	1.195	1.210	.324
Alcohol	2.790	1.883	.139
Binge Drinking	-1.646	1.512	.277
Other Drugs	2.844	1.328	.033

5.4.10. Associations between Different Measures of Cannabis Use and Psychotic-Like Experiences: Preliminary Analysis

Firstly, analyses were conducted to identify the strength of the associations between cannabis use and psychotic-like experiences taking into account continuous variables. Pearson's correlation analyses were conducted, results showed no correlation between the QFSA and the total score of psychotic-like experiences (R^2=.016, p=.692).

5.4.11. Psychotic-Like Experiences, Lifetime Cannabis Use and Use of Other Drugs

Hierarchical linear regression models were conducted to identify associations between psychotic-like experiences, lifetime cannabis use and use of other drugs. No sociodemographic characteristics were included in the initial unadjusted models as no associations were previously found with psychotic-like experiences.

Table 5.10 Linear Regression Model: Total Score Psychotic-Like Experiences, Lifetime Cannabis Use and Use of Other Drugs

Model 1	**Unstandardized B**	**SE**	**p**
Lifetime cannabis use	2.18	1.17	.064
Model 2			
Lifetime cannabis use	.573	1.25	.645
Lifetime tobacco use	4.08	1.14	.000*
Model 3			
Lifetime cannabis use	-.526	1.31	.688
Lifetime tobacco use	3.64	1.15	.002*
Lifetime use of any illicit drugs	3.52	1.36	.010*

Model 4			
Lifetime cannabis use	-.604	1.31	.646
Lifetime tobacco use	3.10	1.22	.012*
Lifetime use of any illicit drugs	3.38	1.37	.014*
Lifetime use of alcohol	1.86	1.47	.206
Model 5			
Lifetime cannabis use	-.716	1.32	.587
Lifetime tobacco use	2.82	1.26	.026*
Lifetime use of any illicit drugs	3.22	1.38	.020*
Lifetime use of alcohol	1.73	1.48	.242
Lifetime use of e-cigarettes	1.08	1.18	.361

In the hierarchical linear regression model with psychotic-like experiences total score as outcome and lifetime cannabis use as main predictor, while controlling for confounding variables which were previously found to be associated with psychotic-like experiences, results showed that participants reporting lifetime tobacco use scored up to 2 points higher in the PRIME Screen Questionnaire than non-tobacco users (B=2.82, SE=1.26, p=.026). Furthermore, participants reporting lifetime use of any illicit drugs scored up to 3 points higher in the questionnaire than participants reporting non-use of illicit drugs (B=3.22, SE=1.38, p=.02).

5.4.12. Association between Cannabis Use and Psychotic-Like Experiences Controlling for Sociodemographic Characteristics and Use of Other Drugs

Multiple linear regression analyses were conducted to identify significant associations between different patterns of cannabis use and psychotic-like experiences while

controlling for sociodemographic factors and use of other drugs. These analyses are the core and main interest of the present study. Results are summarised in Table 5.11.

Significant associations were found between cannabis use and psychotic-like experiences, firstly with lifetime tobacco use (B=2.94, SE=1.29; p=.025), as well as the use of illicit drugs (B=3.34, SE=1.39; p=.016) (Table 5.11).

Table 5.11 Association between QFSA and Psychotic-Like Experiences Adjusted for Sociodemographic Characteristics and Use of Other Drugs: Multiple Linear Regression Analyses

	B	**SE**	**p**
QFSA	-1.60	1.29	.218
Age	-.28	.55	.615
Gender	-1.70	1.11	.127
Ethnicity	.425	.78	.587
Socioeconomic Level	.450	.90	.617
Tobacco*	2.94	1.29	.025*
E-cigarettes	1.35	1.22	.268
Alcohol	2.74	1.88	.146
Binge Drinking	-1.48	1.52	.329
Illicit Drugs*	3.34	1.39	.016*

5.5. Summary

Prevalence of psychotic-like experiences in the adolescent student sample was of 20.4%, similar to what research has found in the general adolescent population (Kelleher et al., 2012). Cannabis use was more prevalent among males than females and

was significantly associated with lifetime use of licit and illicit drugs. Lastly, psychotic-like experiences were associated with lifetime tobacco and use of licit and illicit drugs.

No significant associations between cannabis use and psychotic-like experiences. A number of reasons may explain the nature of these results. First, the quantity and frequency of cannabis reported by participants in the school sample was very low. Most participants reported using once in their lifetime and using less than one joint on a typical occasion. Research has shown that one of the main patterns of cannabis use linked with psychotic-like experiences is high quantity and high frequency of use (Fergusson, D., et al., 2003), which would then explain the non-significant associations in the present study. However, it could be a possibility that in Mexico, low frequency of cannabis use might not be associated with the development of psychotic-like experiences. This could be due to type of cannabis or method of use (without tobacco), nevertheless, further research is needed to fully understand the nature of the obtained results.

The main interest of the present study, and one of the main hypotheses of this project was that higher scores of psychotic-like experiences would be observed in adolescents using cannabis than in non-using adolescents. Results did not corroborate said hypothesis once all sociodemographic factors and use of other drugs were controlled for. Furthermore, higher levels of psychotic-like experiences were not observed in high-potency cannabis users than in low-potency cannabis users or non-using adolescents. This hypothesis, as the previously mentioned, was not corroborated as there were no significant differences between prevalence of psychotic-like experiences and types of cannabis used.

Small sample size of participants using cannabis frequently is something to be considered. Power analyses were conducted to ensure that the sample size recruited could detect an association between cannabis use and psychotic-like experiences. Nevertheless, these power analyses were conducted with data extracted from studies that had been conducted in western countries, with larger samples, and prevalence of use considered to detect an association was lifetime cannabis use. Bayesian statistics could be conducted as a possibility to support the null hypothesis.

6. Cannabis Use and Psychotic-Like Experiences in an Adolescent Substance Misuse Clinical Sample in Mexico City

6.1. Introduction

6.1.1. Rationale for Examining Psychotic-Like Experiences in a Substance Misuse Clinical Sample

Research has shown that cannabis use is associated with the presence of psychotic-like experiences (see Chapters 1 and 2). However, studies have mainly been conducted in populations presenting with a first psychotic episode or in the general population. Few studies have focused on substance misuse populations; hence the interest in the present study.

One study in Sweden examining three different samples from a substance misuse treatment service were identified and data were extracted from clinical files, 1,992 participants treated from 1986 to 1971 and followed up to age 50; 1,576 individuals treated from 1980 to 1984 and followed up to age 35 and 180 treated in 2004 followed up to age 22. Each clinical sample was then matched on all sociodemographic characteristics with randomly selected individuals from the general population (Hodgins et al., 2016). Results showed that adolescents treated for substance misuse were at increased risk for developing schizophrenia than participants in the general population, in both males and females (OR=4.24, 95%CI=2.18-8.24; OR=7.04, 95%CI=2.45-2.25) respectively.

This was the only study found through different searches of databases where the population was similar to the one studied in the present study.

6.2. Objectives

To examine potential associations between different measures of cannabis use (frequency of use, quantity of use, quantity by frequency use scales, age of first use, type of cannabis mainly used, preferred method of use) and psychotic-like experiences in a substance misuse clinical sample.

6.3. Methods

Assessments used in the clinical sample were identical to the ones used in the school sample. For in-depth description see Chapter 3.

6.4. Statistical Analysis

Analyses were conducted, as in the previous chapter, using the statistical package IBM SPSS Statistics Version 25. Descriptive statistics were conducted to identify number of participants by age and gender, ethnicity and socioeconomic status. Analyses were conducted to identify mean age of onset of cannabis use, frequency and quantity of use, type of cannabis mainly used and preferred method of use. Chi-square analyses were conducted to identify differences between different patterns of cannabis use and sociodemographic characteristics.

6.4.1. Patterns of Use of Other Drugs and Associations with Psychotic-Like Experiences

Descriptive statistics were conducted to determine prevalence of psychotic-like experiences in the clinical sample, overall and by gender. Furthermore, analyses were conducted to identify if use of other drugs were independently associated with

psychotic-like experiences. Both, continuous and dichotomous variables of the PRIME Screen Questionnaire were included in these analyses. Odds ratio were calculated using a two-by-two contingency table to identify associations between psychotic-like experiences and daily and weekly use of tobacco; daily, weekly and monthly e-cigarette use; daily and weekly alcohol use; every day and weekly binge drinking; daily, weekly and monthly benzodiazepine use; daily, weekly and monthly methamphetamine use and daily, weekly and monthly solvent use.

6.4.2. Independent Associations between Different Patterns of Cannabis Use and Psychotic-Like Experiences

The main interest of the present study was to identify plausible associations between cannabis use and psychotic-like experiences. Odds ratios were calculated using a two-by-two contingency table to examine associations between different measures of cannabis use and psychotic-like experiences (dichotomous measure 40+ positive score). Dichotomous measures of cannabis use included frequent vs. non-frequent cannabis use, quantity of use (less than one or one joint vs. two or more), method of use (water pipe or bong vs. any other) and type of cannabis (herbal-type vs. skunk-type).

6.4.3. Multiple Linear Regression Analyses: Association between Cannabis Use and Psychotic-Like Experiences Controlling for Sociodemographic Characteristics and Use of Other Drugs

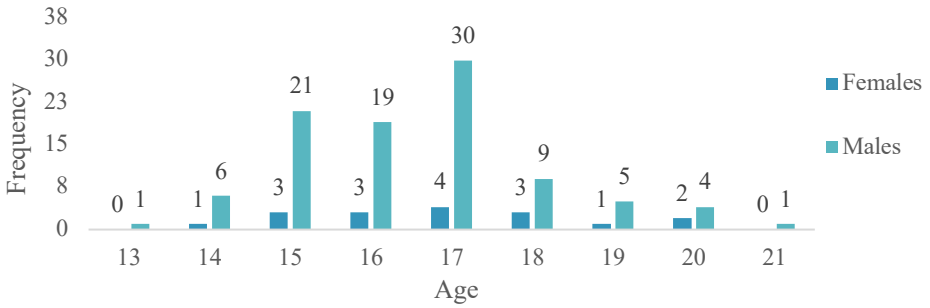
Multiple linear regression models were conducted to identify plausible associations between different measures of cannabis use and psychotic-like experiences while controlling for sociodemographic characteristics and use of other drugs. A linear

regression model was fitted with the total score of the psychotic-like experiences assessment as outcome and the total score of the quantity by frequency scale of cannabis used (QFSA). Age, gender, ethnicity and socioeconomic status and the same variables of use of other drugs included in the logistic analyses were included in the linear model.

6.5. Results

A total of 114 adolescents aged from 13 to 21-years old completed the questionnaires in the clinical sample. Mean age was 16.56 (SD=1.58). A total of 85% (N=96) of participants were male and 15% (N=17) were female. The response rate of the clinical sample was higher than the school sample; 99% of clinic attendees referred to the study consented to participate in the study.

Figure 6.1 Number of Participants by Age and Gender

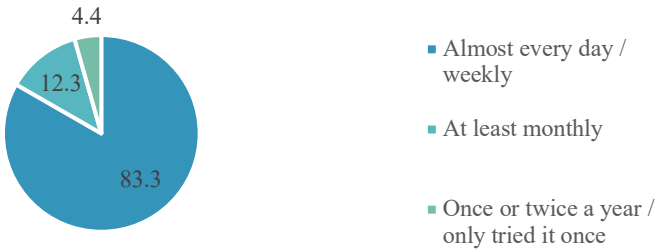


Almost half of the sample identified themselves as Hispanic or Latin (48.7%), followed by African Descent with 24.3% and 20% as Caucasian. Five-point two percent identified themselves as being part of 'Other' ethnicity. More than half of participants scored in socioeconomic level C+/C/C- (51.3%), 32.2% in D+/D/E and 16.5% in level A/B.

6.5.1. Frequency of Cannabis Use

Mean age of first use of cannabis was 13.75 (SD=1.64), with age of onset starting from 9 up to 17 years old. Frequency of cannabis use among the clinical sample was relatively high, although not as high as expected, (see Figure 6.2) with 83.3% reported using cannabis every day or weekly. Every day or almost daily use was reported by 58.3% of males and 58.8% of females. These data are not presented separated by gender as chi-square tests revealed no significant differences in frequency of cannabis use by gender (X^2=4.27, df=5; p=.511), ethnicity (X^2=12.70, df=15, p=.625) or socioeconomic level (X^2=14.60, df=25, p=.950). However, significant differences were found in frequency of cannabis use by age (X^2=62.83, df=40; p=.012) indicating that older participants were more likely to use cannabis daily or almost daily.

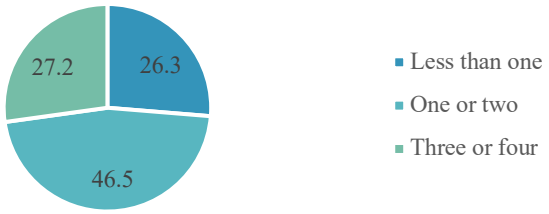
Figure 6.2 Frequency of Cannabis Use



6.5.2. Quantity of Cannabis Use

Just over one quarter of the sample reported using three to four joints on any typical occasion (27.2%) and almost half (46.5%) reported using one or two joints (Figure 6.3). There were no significant differences in quantity of cannabis use by age (X^2=52.06, df=40; p=.096), gender (X^2=3.87, df=5; p=.568), ethnicity (X^2=9.45, df=15, p=.853) or socioeconomic level (X^2=26.05, df=25, p=.405).

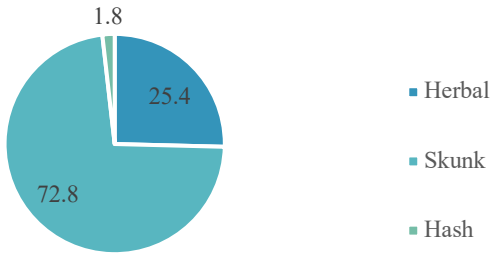
Figure 6.3 Quantity of Use: Number of Joints



6.5.3. Types of Cannabis Mainly Used

Regarding type of cannabis, skunk had the highest prevalence of use among participants with 72.8% (83 participants) reporting skunk as the type mainly used. As shown in Figure 6.4 herbal cannabis was reported by 25.4% (29 participants) and only 1.8% (2 participants) reported hash as the mainly type of cannabis used. Chi-square analyses with the original 3 category variable showed no significant differences between type of cannabis mainly used and age (X^2=16.59, df=16, p=.413), gender (X^2=.432, df=2, p=.806), ethnicity (X^2=4.85, df=6, p=.564) or socioeconomic level (X^2=9.41, df=10, p=.494).

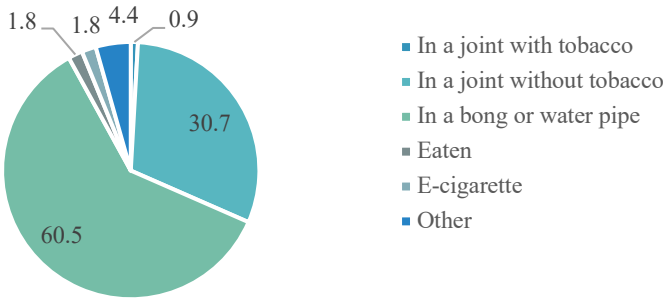
Figure 6.4 Type of Cannabis Mainly Used



6.5.4. Method of Use

Water pipe or bong was the preferred method of use, followed by 30.7% reporting using cannabis in joints without tobacco. All other preferred methods of use were much lower (see **Error! Reference source not found.**). Chi-square analyses showed no differences between preferred method of use and age (X^2=39.21, df=40, p=.506), gender (X^2=5.81, df=5, p=.326), ethnicity (X^2=10.28, df=15, p=.802) or socioeconomic level (X^2=26.78, df=25, p=.367).

Figure 6.5 Preferred Method of Use



6.5.1. Cannabis Use Experience Questionnaire, Sociodemographic Characteristics and Use of Other Drugs

Analyses were conducted to identify differences between the cannabis use experience questionnaire, sociodemographic characteristics and use of other drugs. No significant differences were found according to the analyses of variance conducted (

Table 6.1).

Table 6.1 Cannabis Use Experiences Questionnaire Mean Scores by Sociodemographic Characteristics and Use of Other Drugs

	%	Mean	SD	F	df	p
Age				.142	3	.935
<15	28.7	10.84	2.70			
16	20	10.65	2.42			
17	29.6	10.97	3.10			
18-19	21.7	11.24	4.48			
Gender				3.60	1	.060
Female	14.8	12.29	4.06			
Male	84.3	10.71	3.00			
Ethnicity				2.96	3	.035*
Caucasian		9.00	1.27			
Hispanic or Latin		10.34	2.58			
African Descent		11.21	3.00			
Other		12.26	4.37			
Socioeconomic Level				.084	2	.919
A/B	16.5	1.11	3.32			
C+/C/C-	51.3	10.81	3.49			
D+/D/E	32.2	11.03	2.72			
Use of Other Drugs						
Tobacco Use At Least Weekly	50.9	11.26	3.55	.993	1	.321
Binge Drinking At Least Weekly	20.2	11.74	2.14	1.85	1	.176
Solvent Use At Least Monthly	21.1	11.96	3.51	3.20	1	.077

Benzodiazepine Use At Least Monthly	9.6	12.00	2.45	1.36	1	.245
Use of Other Drugs At Least Monthly	6.1	11.57	2.51	.297	1	.587

Table 6.2 Patterns of Cannabis Use and Mean Scores of the Cannabis Experiences Questionnaire

Age of First Use	**%**	**Mean**	**F**	**df**	**p**
Early Onset (9 – 14)	73%	11.18	1.22	1	.271
Later Onset (15 – 17)	41%	10.49	2.92		
Frequent vs. Non-Frequent		11.36	2.89		
Frequent Use (daily)	57.9%	10.33	.017	1	.090
Non-Frequent Use (weekly to only once)	42.1%	11.46	1.13		
Quantity of Use (Joints)		10.45	1.22		
Two or more	47.4%	10.90	2.92	1	.092
Less than one or one	52.6%	10.98	2.89		
Routes of Administration		10.73	.017		
Bong or water pipe	60.5%	11.45	1.13	1	.898
Any Other	39.5%	11.18	1.22		
Type of Cannabis		10.49	2.92		
Skunk	72.8%	11.36	2.89	1	.290
Herbal or Hash	27.2%	10.33	.017		

6.5.2. Patterns of Cannabis Use and Cannabis Use Experience Questionnaire

Analysis of variance was conducted to identify if different patterns of cannabis use were significantly associated with higher levels of unpleasant effects experienced by participants after the use of cannabis (Table 6.2). No significant differences were found in mean scores of the CEQ and different patterns of cannabis use, indicating that participants experienced similar levels of unpleasant effects disregarding patterns of cannabis use.

Table 6.3 Lifetime Use, Age of Onset and Frequency of Use of Other Drugs

	Lifetime Use %(N)	Mean Age of Onset	Every Day-Almost Daily	Once-Twice a Week	Once-Twice a Month	Less than Once a Month	Once-Twice a Year	Just Tried it Once
Tobacco	91.2 (104)	12.96	28.9	21.9	13.2	9.6	7.0	12.3
E-cigarettes	67.5 (77)	14.36	3.5	7.9	5.3	13.2	14	25.4
Alcohol	93 (106)	13.39	2.6	21.1	31.6	17.5	13.2	7.9
Binge Drinking	84.2 (96)	13.39	2.6	17.5	22.8	21.1	10.5	8.6
Cocaine	48.2 (55)	15.29	2.6	6.1	9.6	6.1	9.6	14
Crack	33.3 (38)	15.37	2.6	3.5	7.0	4.4	6.1	10.5
Solvents	47.4 (54)	14.57	6.1	9.6	5.3	4.4	11.4	12.3
Hallucinogens	37.7 (43)	15.48	0	2.6	6.1	9.6	10.5	10.5
Ecstasy	14.9 (17)	15.67	0	.9	1.8	0	6.1	8.8
Benzodiazepines-Sleeping Pills	23.7 (27)	14.75	8.8	0	.9	.9	3.5	9.6
Opioids	2.6 (3)	14.60	0	.9	0	.9	.9	1.8
Heroin or Opium	5.3 (6)	15	0	0	0	1.8	0	4.4
Amphetamines-Methamphetamines	19.3 (22)	15.40	0	3.5	1.8	4.4	4.4	5.3
Other Drugs	13.2 (15)	15.67	1.8	.9	3.5	.9	3.5	4.4

**Values shown as % and (N) in lifetime use*

6.5.3. Patterns of Use of Other Drugs: Licit and Illicit

Mean age of onset of alcohol use was 13.39 years old and for 12.96 for tobacco use, prevalence of lifetime use of alcohol was reported by 93% of participants and 91.2% reported lifetime tobacco use (

Table 6.3). Prevalence of daily or almost daily use of tobacco was reported by 28.9% of

	Lifetime Use %(N)	Mean Age of Onset	Every Day-Almost Daily	Once-Twice a Week
Tobacco	91.2 (104)	12.96	28.9	21.9
E-cigarettes	67.5 (77)	14.36	3.5	7.9
Alcohol	93 (106)	13.39	2.6	21.1
Binge Drinking	84.2 (96)	13.39	2.6	17.5
Cocaine	48.2 (55)	15.29	2.6	6.1
Crack	33.3 (38)	15.37	2.6	3.5
Solvents	47.4 (54)	14.57	6.1	9.6
Hallucinogens	37.7 (43)	15.48	0	2.6
Ecstasy	14.9 (17)	15.67	0	.9
Benzodiazepines-Sleeping Pills	23.7 (27)	14.75	8.8	0
Opioids	2.6 (3)	14.60	0	.9
Heroin or Opium	5.3 (6)	15	0	0
Amphetamines-Methamphetamines	19.3 (22)	15.40	0	3.5
Other Drugs	13.2 (15)	15.67	1.8	.9

participants. Among illicit drugs, powder cocaine was the most commonly used with 48.2% reporting lifetime use, followed by solvents with 47.4%. Furthermore, daily use of benzodiazepines was reported by 8.8% and 6.1% reported daily solvent use. Mean age of first use of any illegal drug was 15.18 years old. Overall, it can be observed that frequent use of illicit drugs was, to some degree, uncommon.

6.5.4. Prevalence of Psychotic-Like Experiences

Prevalence of positive scores in the psychotic-like experiences assessment in the clinical sample was of 27.2%. According to gender, 27.1% of females and 29.4% of men had scored positively in the PRIME Screen Questionnaire. No statistically significant

differences were found by age (X^2=5.62, df=8, p=.690) or gender (OR=.90, 95%CI=.29-2.78). Moreover, no significant differences were found between the total score of the PRIME and ethnicity (X^2=3.10, df=3, p=.377) or socioeconomic level (X^2=2.44, df=5, p=.785).

6.5.5. Associations between Psychotic-Like Experiences and Use of Other Drugs

Analyses were conducted to identify if frequency of use of other drugs were significantly associated with psychotic-like experiences. Significant differences were found in mean scores of the PRIME Screen Questionnaire and daily, weekly and monthly use of benzodiazepines (F=5.66, df=1, 112; p=.019) compared to less frequent use of benzodiazepines. Moreover, statistically significant differences were found in mean scores of the PRIME Screen questionnaire and daily, weekly and monthly use of solvents (F=8.01, df=1, 112; p=.006), compared to less frequent use of solvents **Error! Reference source not found.**.

Table 6.4 Psychotic-Like Experiences and Frequent Use of Other Drugs

	Mean	**F**	**df^1, df^2**	**p**	**Prevalence PLE's (%)**
Tobacco Use					
Daily and Weekly	1.48	.441	1, 104	.523	46.7
Monthly or Less	1.46				
Alcohol Use					
Daily and Weekly	1.50	1.86	1, 112	.176	32.3
Monthly or Less	1.45				
Binge Drinking					
Daily and Weekly	1.51	1.68	1, 112	.198	25.8
Monthly or Less	1.45				
E-cigarette Use					
Daily, Weekly and Monthly	1.50	1.12	1, 112	.292	19.4
Less than Monthly	1.45				

Benzodiazepine Use					
Daily, Weekly and Monthly	1.59	5.66	1, 112	.019*	19.4
Less than Monthly	1.45				
Methamphetamine Use					
Daily, Weekly and Monthly	1.57	1.95	1, 112	.166	6.5
Less than Monthly	1.45				
Solvent Use					
Daily, Weekly and Monthly	1.56	8.01	1, 112	.006*	32.3
Less than Monthly	1.43				

Table 6.5 Patterns of Cannabis Use and Psychotic-Like Experiences

	Mean Scores	**F**	**df^1, df^2**	**p**	**Prevalence PLE's (%)**
Frequent vs. Non-Frequent					
Frequent Use	1.50	5.68	1, 112	.019*	30.3
Non-Frequent Use	1.41				22.9
Quantity of Use					
Two or more	1.52	7.70	1, 112	.007*	31.5
Less than one or one	1.42				23.3
Routes of Administration					
Bong or water pipe	1.44	.94	1, 112	.334	23.2
Any Other	1.49				33.3
Type of Cannabis					
Skunk	1.44	2.88	1, 112	.093	21.7
Herbal or Hash	1.51				41.9
Age of Onset of Cannabis Use					
9 to 14	1.48	1.86	1,112	.175	26
15 to 17	1.43				29.3

6.5.6. Independent Associations between Different Patterns of Cannabis Use and Psychotic-Like Experiences

Analyses were conducted to identify associations between different measures of cannabis use and psychotic-like experiences. Analyses of variance were conducted to identify differences in mean scores of the psychotic-like experiences questionnaire and different patterns of cannabis use. Analyses indicated statistically significant differences between psychotic-like experiences and frequent cannabis use (every day or almost daily) (F=5.68, df=1, 112, p=.019) and using two or more joints on any typical occasion (F=7.70, df=1, 112, p=.007) compared with non-frequent users (from weekly to only tried it once) and participants using less than one or one joint on a typical occasion. Further analyses were conducted to identify if age of onset of cannabis use was significantly associated with age of onset of psychotic-like experiences. Results showed a significant association between age of onset, indicating that participants who starting using cannabis at an earlier age, reported earlier onset of psychotic-like experiences (F=2.25, df=8, 96; p=,030) compared to participants reporting later onset of cannabis use.

	B	**SE**	**p**
QFSA	.003	.002	.104
Age	-.02	.01	.247
Gender	.01	.05	.872
Ethnicity	.04	.02	.074
Socioeconomic Leve	.00	.01	.746
At Least Weekly Tobacco Use	.01	.04	.768
At Least Weekly Binge Drinking	.01	.05	.891
At Least Monthly Benzodiazepine Use	.14	.07	.039*
At Least Monthly Solvent Use	.06	.05	.222

Table 6.6 Cannabis Use and Psychotic-Like Experiences

**QFSA: Quantity by frequency scale any type of cannabis.*

Table 6.7 Type of Cannabis and Psychotic-Like Experiences

	OR	**95%CI**	**p**
Type of Cannabis	.24	.08-.73)	.011*
Age	.96	.69-1.36	.832
Gender	1.36	.32-5.86	.680
Ethnicity	1.42	.80-2.52	.235
Socioeconomic Leve	.84	.63-1.13	.247
At Least Weekly Tobacco Use	.37	.13-1.02	.055
At Least Weekly Binge Drinking	.95	.29-3.08	.927
At Least Monthly Benzodiazepine Use	4.07	.88-18.93	.073
At Least Monthly Solvent Use	2.76	.83-9.20	.099

6.5.7. Associations between Cannabis Use and Psychotic-Like Experiences

Controlling for Sociodemographic Characteristics and Use of Other Drugs

Multiple linear regression analysis including the total scores of the PRIME as outcome and the quantity by frequency scale of any type of cannabis used as main predictor were conducted. No significant associations were found between the total score of the psychotic-like experiences assessment and the total score of the quantity by frequency scale of cannabis use. However, associations remained significant between daily, weekly and monthly use of benzodiazepines and psychotic-like experiences after controlling for sociodemographic characteristics and use of other drugs (B=.14, SE=.07; p=.035), indicating that participants reporting daily, weekly or monthly use of benzodiazepines were more likely to have higher mean scores in the psychotic-like experiences questionnaire than participants reporting experimental or non-use of benzodiazepines.

Furthermore, when including type of cannabis as main predictor, significant associations were found between a positive score in the psychotic-like experiences questionnaire and type of cannabis (OR=.24, 95%CI=.08-.73, p=.011), indicate that participants reporting herbal cannabis as the main type used, were more likely to have a positive score in the PRIME Screen Questionnaire than participants reporting skunk.

6.6. Summary

Overall, mean age of cannabis use onset was (13.8). Skunk-type cannabis was the most reported type in the clinical sample (72.8%) compared to herbal-type cannabis (25.4%). Results derived from these analyses were not expected. Firstly, it was expected that frequent cannabis use, heavy cannabis use, skunk-type cannabis use and the total score of the quantity by frequency scale of cannabis use were significantly associated with psychotic-like experiences before and after controlling for sociodemographic characteristics and use of other drugs.

However, these associations were not found. Initially, frequent cannabis use was significantly associated with the total score of the PRIME Screen Questionnaire, nevertheless in the first stepwise model fitted, where frequent cannabis use was included as the main predictor, followed by sociodemographic characteristics and then, by use of other drugs, with the dichotomous measure of the psychotic-like experiences assessment as outcome, this association did not remain significant. These results were not anticipated, as previous research has shown that increased frequency of cannabis use

is strongly linked to the presence psychotic-like experiences (Fergusson et al., 2003; Mustonen, Niemela, et al., 2018). Similarly, quantity was, initially, significantly associated with psychotic-like experiences when analysed separately, however once the model was fitted this association was no longer significant.

Furthermore, there was a significant association between herbal-type of cannabis and psychotic-like experiences, before and after controlling for sociodemographic characteristics and use of other drugs. This result contradicts previous research regarding type cannabis mainly being used and an increased risk of psychosis (Di Forti et al., 2009). In the final model, where the QFSA was included as the main predictor, in the first block of the stepwise model, before all other variables were included, there was a significant association between the QFSA and the total score of the PRIME Screen Questionnaire. However, this association did not remain significant when all the variables were included. In this linear model the only variable that remained significantly associated with psychotic-like experiences while controlling for sociodemographic factors and use of other drugs was frequent use of benzodiazepines.

One important thing to mention that from the whole sample, only 29 participants reported using 'herbal' type cannabis. This reduces statistical power as the sample size of herbal cannabis users is smaller than participants reporting 'skunk' type cannabis, with 83 participants reporting use of this type of cannabis. There are significant differences between the present study and previous research that may account for these results. Firstly, most studies have been conducted in different clinical populations, e.g. subjects presenting with a first psychotic-episode (Di Forti et al., 2009). Few studies

have been done in adolescents as shown in Chapter 1 and fewer in substance misuse clinical samples (Hodgins et al., 2016). Similar studies, to the best of my knowledge, have never been conducted in Mexico and, furthermore, there is no research regarding different types of cannabis available in Mexico. This is a major limitation as it is difficult to estimate the potency of cannabis in the country and to what extent herbal cannabis is low potency or if its potency is higher than the average of potency in herbal cannabis elsewhere.

7. Discussion

7.1. Introduction

In the final chapter, a discussion of the results will be presented, along with different hypotheses which will attempt to explain the results obtained in the present study. Overall, results were unexpected and, in some ways, contradictory to what has been previously found in similar studies. Results from the systematic review conducted are used to compare and contrast the findings of the present study to what has been previously found. An in-depth examination of the methodology and results of these studies is presented to identify how the present study may differ from previous research.

Additional results from both samples are summarised to better understand patterns of cannabis use and psychotic-like experiences and to identify associations with covariates. This is considered relevant as, although there were no associations between cannabis and psychotic-like experiences found, other associations were identified. And although these were not part of the main objectives of this project, it is important to consider them for future research, prevention and public policies. Lastly, implications for future research are discussed, with focus on the different outcomes obtained from the study. Implications of findings for public policies are suggested and recommendations are made.

7.2. Summary of Findings: Cannabis Use and Psychotic-Like Experiences

No associations were found between different patterns of cannabis use and psychotic-like experiences in the adolescent student sample. Not when associations were looked at independently, nor when full adjusted models were conducted with different patterns and measures of cannabis use as main predictor, psychotic-like experiences as main outcome and sociodemographic characteristics and use of other drugs as covariates (Table 7.1).

On the other hand, in the adolescent substance misuse clinical sample significant differences were found in the total score of the PRIME Screen Questionnaire and frequent vs. no frequent cannabis use. Quantity of use was also significantly associated with psychotic-like experiences, with higher mean scores in participants reporting use of two or more joints on any typical occasion compared to participants reporting one or less than one joint. However, these associations disappeared once sociodemographic characteristics and use of other drugs were included in the full adjusted model (Table 7.1). Moreover, in the substance misuse clinical sample, type of cannabis used was significantly associated with the psychotic-like experiences questionnaire, when examined independently and after controlling for all other confounding variables and covariates. However, the association that remained was negative, which indicates that herbal-type cannabis users were more likely to obtain a positive score in the PRIME Screen Questionnaire than participants using skunk-type cannabis. These results are contradictory to what has been previously reported regarding type of cannabis and psychotic-like experiences.

Analyses were conducted in the substance misuse clinical sample to identify associations between age of onset of cannabis use and age of onset of psychotic-like experiences. Results showed that participants with earlier onset of cannabis had earlier onset of psychotic-like experiences. This result supports previous studies which have found that early onset of cannabis use might impact on an earlier onset of psychotic-like experiences or first episode psychosis (Bagot et al., 2015; Di Forti et al., 2014). However, one of the studies referred to previously, was conducted in a sample of patients presenting for first episode psychosis, which differs from the clinical sample in the present study; therefore, comparisons should be made with caution. Table 7.1 show variables included in the adjusted model and if a significant association was found.

Due to the unexpectedness of the results obtained, a number of different hypothesis are provided to attempt to explain why the difference between results in present study compared to previous studies which examined the association between cannabis use and psychotic-like experiences conducted in adolescent populations.

Table 7.1 Significant Associations between Cannabis Use and Psychotic-Like Experiences in Adjusted Models

Student Sample		**Substance Misuse Clinical Sample**	
Cannabis Use	**A**	**Cannabis Use**	**A**
Lifetime	(-)	Frequent	(-)
Monthly	(-)	Heavy	(-)
Type	(-)	Type*	(+)
QFSA	(-)	QFSA	(-)
Sociodemographic Characteristics		**Sociodemographic Characteristics**	
Age	(-)	Age	(-)
Gender	(-)	Gender	(-)
Ethnicity	(-)	Ethnicity	(-)
Socioeconomic Level	(-)	Socioeconomic Level	(-)
Use of Other Drugs: Lifetime		**Use of Other Drugs: Frequent**	
Tobacco	(-)	Tobacco	(-)
E-cigarettes	(-)	Binge Drinking	(-)
Alcohol	(-)	Benzodiazepines	(+)
Binge Drinking	(-)	Solvents	(-)
Illicit Drugs	(+)		

A=Associations; (-)=no association; (+)=positive association;

**Association with herbal-type cannabis*

7.3. Differences in Patterns of Use and Type of Cannabis

7.3.1. Prevalence of Lifetime and Frequent Cannabis Use

One hypothesis which might serve as explanation to the results obtained in the adolescent student sample is that lifetime prevalence of cannabis use is not as high as prevalence of use reported in previous studies. Results in the present study showed a lifetime prevalence of cannabis use of 29.6% in the adolescent student sample. Below, a table with studies previously conducted in an adolescent population which examined the associations between cannabis use and psychotic-like experiences is presented; alongside, prevalence of lifetime cannabis use can be observed.

As shown in **Error! Reference source not found.** prevalence of lifetime cannabis use in the adolescent student sample of present study is not markedly lower than lifetime prevalence reported in previous studies. Around a third of the studies reported a similar lifetime prevalence of use. Furthermore, when examining prevalence of lifetime cannabis use and the association between cannabis use and psychotic-like experiences in those studies, it was found that some studies which reported lower prevalence of use did find a significant association (Henquet et al., 2005; Stefanis et al., 2004; van Gastel et al., 2012). Therefore, differences in prevalence of lifetime cannabis use between the present study and previous research cannot serve as a plausible explanation for the results obtained regarding the lack of association between cannabis use and psychotic-like experiences in the adolescent student sample.

An additional hypothesis regarding patterns of cannabis use is that frequency of use may have been lower than in previous studies. To examine this hypothesis **Error! Reference source not found.** describes the definition and prevalence of frequent cannabis use in each of the studies reported in the systematic review. In the present study, frequent use (monthly to daily use) among lifetime cannabis users was reported by 33.3%; and by 10.7% in all the adolescent student sample.

Overall, frequency of cannabis use among previous studies is not noticeably different compared to the frequency of use reported in the present study; and in comparison to some of the studies presented (Arseneault et al., 2002; Miettunen et al., 2018; Miettunen et al., 2008), frequency of use in this adolescent sample was higher. Nevertheless, these studies did find an association between cannabis use and psychotic-like experiences. Therefore, the lack of association between cannabis use and psychotic-like experiences could not be explained either from a low prevalence of lifetime or frequency of cannabis use.

However, sample size is something to be considered. In the present study, power analyses were conducted to ensure that the sample size recruited could detect an association between cannabis use and psychotic-like experiences. Nevertheless, these analyses were conducted with data extracted from studies that had been conducted in western countries and with larger samples. As discussed below, cultural differences could be a contributor on results obtained.

7.3.2. Preferred Method of Use by Country

Another hypothesis to account for results obtained, is that the preferred method of cannabis use in Mexico is different from the preferred method of use in countries where previous studies have been conducted. Most studies have been conducted in countries where cannabis is mainly smoked with tobacco (Gage et al., 2014; Jones et al., 2018; Mackie et al., 2013), however this is not how cannabis is mainly used in Mexico. The most prevalent method of use reported in the present study was via water pipe or bong, with 53.1% of participants reporting this as their preferred method of use and 20.3% in a joint without tobacco in the student sample. Similar to this, 60.5% of participants in the clinical sample reported water pipe or bong as their preferred method of use, followed by 30.7% in a joint without tobacco.

Previous research has shown that in Mexico and the United States of America, water pipe and/or bong are the most prevalent method of use among cannabis users and it is mainly used without tobacco (Hindocha et al., 2016). This is an outstanding difference, and one that could help in the understanding of the results obtained as tobacco has been associated with psychotic-like experiences and psychotic disorders, such as schizophrenia (Gurillo, Jauhar, Murray, & MacCabe, 2015). The direction of the association is still in debate, however there is a considerable amount of research in this area which undoubtedly show that there is an association between tobacco use and different spectrum of psychosis (Gurillo et al., 2015).

Error! Reference source not found. lists the different countries where studies examining the association between cannabis use and psychotic-like experiences in

adolescents have been conducted and the most prevalent method of cannabis used. From the twenty-seven studies included in the systematic review, only eight studies were conducted in countries where, similar to Mexico, cannabis is used without tobacco: New Zealand, United States of America and Canada (Anglin et al., 2012; Arseneault et al., 2002; Bechtold et al., 2016; Bourque et al., 2016; Fergusson et al., 2003; Jones et al., 2017; Leadbeater et al., 2019; Levy & Weitzman, 2019).

A study recently conducted in the United States which examined the association between cannabis use and "psychosis spectrum" found that once confounds were adjusted for, cannabis use by itself was not significantly associated with an increase of being classified as part of the psychosis spectrum (Jones et al., 2017), however, the combination of tobacco and cannabis use was. Furthermore, one study conducted in the United Kingdom, a country where cannabis is mainly used with tobacco, examined the associations between cannabis use, cigarette use and psychotic-like experiences. Results showed that in the adjusted model, with cannabis use as main predictor and psychotic-like experiences as outcome, the association between cannabis use with psychotic-like experiences decreased when controlling for frequency of cigarette use and use of other drugs and was no longer significant. However, when the model included cigarette use as main predictor and cannabis use was controlled for, even when the association dropped, cigarette use and psychotic-like experiences remained significantly associated (Gage et al., 2014).

It can be observed in Table 7.2 that most studies did not find the same results. A large variability among studies and findings can be observed. Moreover, each study assessed

cannabis use and psychotic-like experiences outcome differently, which may account for the differences in findings. Might be of interest to develop and structure a standardised single measure of cannabis use, similar to the one we currently have for alcohol use. Similarly, structuring or coming to an agreement of using one specific measure of psychotic-like experiences or psychotic outcome could help to homologise methodology and findings.

These studies could help to explain the unexpected results obtained. Both were conducted in adolescents and both examined the same associations assessed in the present study. Particularly when taking into account the results summarised in the section of "Additional Findings", it can be observed that one of the only significant associations that remained with psychotic-like experiences, with all different measures of cannabis use as main predictor in the fully adjusted model in the student sample was with tobacco use.

Table 7.2 Studies included in Systematic Review: Cannabis Use and Psychotic-Like Experiences in Adolescents

Author, Year & Country	Prevalence Cannabis Use		Method of Use	+ Association			Other Drugs
	Lifetime	Frequent/Heavy		A	E	C	
Arseneault et al. 2002, New Zealand	31.3%	3.8%	Joint / bong with tobacco	-	X	-	X
Fergusson et al. 2003, New Zealand	10%	10%	Joint / bong with tobacco	-	-	X	X
Stefanis et al. 2004, Greece	4.9%	1.5%	NR	X	X	X	X
Henquet et al. 2005, Germany	13.1%	NR	Joint with tobacco	X	-	X	X
Ferdinand et al. 2005, Netherlands	23.3%	NR	Joint with tobacco	X	-	-	-
Konings et al. 2008, Trinidad y Tobago	21%	10%	NR	-	X	-	X
Miettunen et al. 2008, Finland	5.6%	0.9%	NR	X	-	X	X
Hides et al. 2009, Australia	9.5%	2.2%	Bong / joint with tobacco	-	-	X	X
Kuepper et al. 2011, Germany	13%	28%	Joint with tobacco	X	-	X	X
Schubart et al. 2011, Netherlands	66%	25%	Joint with tobacco	X	X	-	-
Roessler et al. 2011, Switzerland	NR	NR	Joint with tobacco	X	-	-	X
Van Gastel et al. 2011, Netherlands	14%	1.5%	Joint with tobacco	X	-	-	-
Anglin et al. 2012, USA	70%	17.1%	Pipe / bong without tobacco	-	X	-	X
Griffith-Lendering et al. 2012, Netherlands	5.8%	1.3%	Joint with tobacco	X	-	-	-
Mackie et al. 2013, UK	25%	11%	Joint with tobacco	X	-	-	-
Gage et al. 2014, UK	27.4%	3.3%	Joint with tobacco	-	-	-	X
Bechtold et al. 2016, USA	NR	27%	Pipe / bong without tobacco	-	-	X	X
Bourque et al. 2017, Canada	8.9%	NR	Joint / pipe without tobacco	-	-	X	-
Jones et al. 2017, USA	28%	5%	Pipe / bong without tobacco	-	-	-	-
Shevlin et al. 2017, Denmark	31.6%	NR	Joint with tobacco	-	-	-	X
Jones et al. 2018, UK	NR	NR	Joint with tobacco	X	X	-	-
Mustonen et al. 2018, Finland	5.7%	1%	NR	-	-	X	X
Albertella et al. 2018, Australia	35%	13%	Bong / joint with tobacco	-	X	X	X
Leadbeater et al. 2018, Canada & USA	36%	10%	Pipe/ bong/ joint without tobacco	-	-	X	-
Bernardini et al. 2018, Brussels	46.3%	35%	Joint with tobacco	X	-	-	-
Levy et al. 2019, USA	52.1%	47.9%	Pipe / bong without tobacco	X	-	-	-
Fonseca-Pedrero et al. 2019, Spain	23.7%	6.5%	Joint with tobacco	-	-	-	-

+ (Positive) Association: A=Any cannabis use, E=Early onset, C=Cumulative Use; Other drug use is marked with and X if included as a covariate

7.3.3. Cumulative and Early Onset of Cannabis Use

One of the main findings that research has shown when examining cannabis use and psychotic-like experiences is that early onset is an important factor that strengthens the association when found. And similarly, this has been shown with cumulative use, with studies showing that there is a linear association where for every increase in cannabis use there is an increase in risk of psychotic-like experiences.

Some studies included in the systematic review found that the association between cannabis use and psychotic-like experiences, was limited to either earlier onset of cannabis use, with later onset not associated, or to cumulative and persistent use. Three studies found the association when cannabis use was early onset, and in seven the association only remained with cumulative use of cannabis (see **Error! Reference source not found.**).

These results confirm the cumulative hypothesis, where research has shown that risk of presenting psychotic-like experiences increases linearly with the quantity and frequency of cannabis use (Bourque et al., 2016; Henquet et al., 2005; Miettunen et al., 2008; Mustonen, Niemela, et al., 2018; van Gastel et al., 2012). Furthermore, as the present study was cross-sectional, cumulative use of cannabis was not assessed.

7.3.4. Type of Cannabis

Another unexpected finding was the association between herbal-type cannabis and psychotic-like experiences in the fully adjusted model in the adolescent substance misuse clinical sample. Given that there has been no research into cannabis potency in Mexico, it is very difficult to know accurately if what participants identified as 'herbal' is really low potency cannabis.

Research has shown that different types of cannabis confer different level of risk of reporting psychotic-like experiences. Normally, skunk-type cannabis or cannabis with high levels of THC has the highest risk of presenting PLE's. (Di Forti et al., 2015). Furthermore, experimental studies have continuously showed that THC increases acute levels of psychotic-symptoms (D'Souza et al., 2004; Morgan & Curran, 2008; Morgan et al., 2018) and produces psychomimetic-like experiences.

This is why it is so unexpected and difficult to explain this particular result. A possible explanation could be that the type of cannabis participants use looks similar to the pictures provided, but that does not necessarily mean that that type of cannabis is low potency. The present study was designed considering previous research conducted in Europe and the US where 'herbal cannabis' or 'grass' is low potency, however, without research on cannabis potency in Mexico, it is difficult to accurately estimate the content of THC and CBD in cannabis.

7.4. Inclusion of Covariates and False Positives

Another possible explanation for the results obtained in the present study is that the adjustment of all the covariates included attenuated the strength of the association. Some studies have initially found a significant association between cannabis use and psychotic-like experiences; however, once adjustments were made to the final models these associations disappeared or significantly attenuated. The variable which produced the most amount of attenuation was use of other illicit drugs.

For instance, a study where lifetime cannabis use was associated with lifetime psychotic-like experiences, there was no control for confounding variables, e.g. use of other drugs (Ferdinand et al., 2005). Similarly, another study conducted in the Netherlands, found that amount of cannabis was associated with psychotic experiences, with higher amounts showing higher risk of scoring in the highest 10% of the psychotic-like experiences assessment, however no adjustment for use of other drugs was made in the complete sample (Schubart et al., 2011).

Moreover, a study recently conducted found no evidence of association between cannabis use alone and psychotic-like experiences after adjusting for confounding factors. Researcher found that it was the interaction of cannabis with other drugs that conferred significant risk for psychotic-like experiences results (Jones et al., 2017).

Twelve studies included in the systematic review did not control for use of other illicit drugs. Of those studies most found a significant association between cannabis use and

psychotic-like experiences (**Error! Reference source not found.**). It has been shown that when use of other illicit drugs is controlled for, the association tends to decrease. Possibly, one of the reasons all these studies did find a significant association is because they did not take into account use of other illicit drugs when conducting the analyses. This could explain why in the present study, no association between cannabis and psychotic-like experiences was found.

On the other hand there have been studies that did control for use of other drugs and still found a significant association between cannabis use and psychotic-like experiences (Henquet et al., 2005; Kuepper et al., 2011; Mackie et al., 2013; Miettunen et al., 2008; Rossler et al., 2007; Stefanis et al., 2004). When studies have reported adjustment for use of other illicit drugs, the association between cannabis use and psychotic-like experiences tends to attenuate. This can be observed in **Error! Reference source not found.**, where is shown that in only five studies that did control for use of other drugs found a significant association between any use of cannabis and psychotic-like experiences.

7.5. Are unexpected results due to cultural differences in prevalence or understanding of psychotic-like experiences in Mexico?

Another possible explanation for the unexpected results may due to cultural differences. Most of the previous research has been conducted in countries culturally different from Mexico, mainly in Europe and the United States. It is possible that prevalence of psychotic-like experiences differs in Mexico compared to other countries and that the understanding of these experiences' changes across different cultures.

For example, there are certain beliefs and cultural traditions in Mexico which differ significantly from Western countries, e.g. 'Day of the Death'. Were it is believed that once a year, people who have died come to visit and an offering is set for them, including food, sweets and personal belongings of the ones who have died. This might seem to some degree delusional to other cultures, however it is a tradition that has remained in Mexico for centuries. The flexibility or openness in these ideas might increase in traditional western assessments the prevalence of psychotic-like experiences among the Mexican population. Therefore, a comparison on prevalence of psychotic-like experiences in this study and in other countries is made.

Prevalence of psychotic-like experiences in the school sample was 20.4%, this was in line with previous international research, where it has been found that prevalence of psychotic-like experiences in the general population is of approximately 20% (Kelleher et al., 2012; van Os et al., 2009). Prevalence of psychotic- like experiences in the substance misuse clinical sample was 27.2%, higher than in the school sample, nevertheless expected. However, as shown above, prevalence of psychotic-like experiences in the student sample was not higher that what has been found in previous results, therefore it is unlikely that the unexpected results were due to cultural differences and perceptions on psychotic-like experiences. Furthermore, the reliability analyses conducted to the PRIME Screen Questionnaire support that the Spanish version used in the study is reliable. As previously mentioned, prevalence of psychotic-like experiences in the clinical sample was notably higher, however, this could easily be explained by the misuse of psychoactive substances (Riggs, Levin, Green, & Vocci, 2008).

7.6. Additional Findings

7.6.1. Sample Characteristics

7.6.1.1. Adolescent Student Sample

The mean age of the school sample was 16.51 (SD =1.05) and the median 17. The response rate of the school sample was 95% as students were happy to participate. Regarding ethnicity, participants mainly indicated Hispanic or Latin as their ethnicity with 60.2% identifying themselves in this category, followed by African-Descent with 25.3%, followed by 6.5% as Caucasian and 6% as Other. Regarding socioeconomic level in the school sample 62% scored as being part of level C+/C/C-, followed by 21.9% in level D+/D/E and 16% in socioeconomic level A/B.

Higher prevalence of lifetime cannabis use was observed among participants in socioeconomic level A/B and although these differences are not statistically significant, it is noteworthy to mention that these results are not the norm, with previous research indicating that populations in lower socioeconomic levels usually have higher prevalence of drug use than populations in higher socioeconomic levels (Daniel et al., 2009). Furthermore, participants in higher socioeconomic levels were more likely to use cannabis more frequently than participants in lower socioeconomic levels. Different reports that have been referenced to in the present study describe numerous data, the manuscript even report having included a socioeconomic questionnaire in the survey, however, there were no data reported regarding these associations. To the best of my knowledge there is no available data regarding socioeconomic level and cannabis use in Mexico.

7.6.1.2. Adolescent Substance Misuse Clinical Sample

A total of 114 adolescents aged from 13 to 21-years old completed the questionnaires in the clinical sample. Mean age was 16.56 (SD=1.58). A total of 85% (N=96) of participants were male and 15% (N=17) were female. The response rate of the clinical sample was higher than the school sample; 90% of clinic attendees referred to the study consented to participate in the study. Almost half of the sample identified themselves as Hispanic or Latin (48.7%), followed by Africa Descent with 24.3% and 20% as Caucasian. Five-point two percent identified themselves as being part of 'Other' ethnicity. More than half of participants scored in socioeconomic level C+/C/C- (51.3%), 32.2% in D+/D/E and 16.5% in level A/B.

7.6.2. What other factors were associated with cannabis use?

7.6.2.1. Adolescent Student Sample

Significant association were found between the total score of the QFSA and lifetime tobacco use, lifetime e-cigarette use, lifetime binge drinking and lifetime use of illicit drugs independently of sociodemographic characteristics and use of other drugs. Furthermore, participants reporting lifetime use of cannabis were more likely to be male, binge drink, use tobacco, e-cigarettes and other illicit drugs than non-lifetime cannabis users. Additionally, at least monthly cannabis use was associated with gender, socioeconomic level, lifetime use of e-cigarettes and lifetime use of any illicit drug. Indicating that males were two times more likely than women to report at least monthly cannabis use. Participants with higher socioeconomic status had higher prevalence of monthly cannabis use than participants from lower socioeconomic status. Furthermore,

monthly users were two times more likely to report e-cigarette use and seven times more likely to have experimented with any illicit drug in their lifetime.

Significant associations were found between participants using skunk-type cannabis and gender, tobacco, binge drinking and other drugs compared with non-users. Furthermore, when examining associations between skunk type cannabis users vs. users of any other type of cannabis, analyses showed significant associations between skunk users, gender and use of any illicit drugs. These results support previous research that suggest that cannabis users are more likely to use other drugs (Hall, 2016). A comprehensive review recently conducted, numbered three possible explanations for this association: cannabis users have more opportunities to obtain other illicit drugs from where they buy the illegal cannabis, the earlier onset of cannabis use makes the probability of use of other drugs more likely or that the pharmacological effects of cannabis makes users more prone to use other illicit drugs (Hall et al., 2019).

7.6.2.2. Adolescent Substance Misuse Clinical Sample

There was one significant association between frequent cannabis use and frequent use of methamphetamines compared to non-frequent cannabis users, indicating that all participants that reported frequent use of methamphetamines were using cannabis daily. Participants reporting high quantities of cannabis use were more likely to report frequent use of methamphetamines and solvents. Moreover, type of cannabis was significantly associated with daily, frequent use of methamphetamines.

7.6.3. What other factors were associated with psychotic like experiences?

Although no associations were found between cannabis use and psychotic-like experiences once models were adjusted, results showed associations between psychotic-like experiences and use of other drugs. In the student sample, lifetime tobacco use, e-cigarettes and use of illicit drugs were continuously associated with either higher levels in the total score of the PRIME.

Furthermore, in the substance misuse clinical sample, psychotic-like experiences were significantly associated with frequent use of benzodiazepines, and solvents. Benzodiazepines were referred in the questionnaire as tranquillisers, which is the term most widely used in Spanish to refer to benzodiazepines. It would be of interest to know if participants were in fact using benzodiazepines and not anti-psychotic medication or other type of prescriptions. If they were in fact using benzodiazepines it would be of interest to know the reason participants were prescribed this medication, as it could be that they have a more complex diagnose of other mental health problems apart from their substance misuse.

Table 7.3 Associations with Psychotic-Like Experiences

Student Sample Sociodemographic Characteristics		**Substance Misuse Clinical Sample Sociodemographic Characteristics**	
Age	-	Age	-
Gender	-	Gender	-
Ethnicity	-	Ethnicity	-
Socioeconomic Level	-	Socioeconomic Level	-
Use of Other Drugs: Lifetime		**Use of Other Drugs: Frequent**	
Tobacco	+	Tobacco	-
E-cigarettes	+	E-cigarettes	-
Alcohol	-	Alcohol	-
Binge Drinking	-	Binge Drinking	-
Illicit Drugs	+	Benzodiazepines	+
		Methamphetamines	-
		Solvents	+

Results are consistent with previous studies that have found a significant association between psychosis and tobacco use (Gurillo et al., 2015). Research around psychosis and tobacco use has been of interest for many decades, showing that there is a significant association between schizophrenia and tobacco use, and that this association is stronger than with other menta health disorders, e.g. mood disorders (de Leon & Diaz, 2005). The possible mechanisms for tobacco being related to psychosis are several. Initially it was thought that patients were self-medicating, from negative symptoms (Dalack, 1998), to improve cognitive processes or through antipsychotic side effects of smoking (Quigley & MacCabe, 2019). However, recently different hypotheses have been suggested, e.g. shared liability, confounding factors or causal relationship (Quigley & MacCabe, 2019). The association has not been completely understood, but further research in the field continue to prove the existence of this association (de Leon & Diaz, 2005). There were no studies found regarding e-cigarette use and psychosis, however, considering that there has been research around nicotine

and psychosis, this could only confirm that what could be a risk factor in the development of psychotic-like experiences is nicotine (Quigley & MacCabe, 2019).

Furthermore, illicit substance use has been shown to increase prevalence of psychotic-like experiences (Barkus & Murray, 2010; Miettunen et al., 2018). Recently a study conducted in Finland found that solvent use was independently associated with psychosis in adolescents, with 80% of participants using solvents being diagnosed with psychosis (Mustonen, Niemelä, et al., 2018). Solvent use in Mexico started to decline after a prolonged period of time where use was increasing (Villatoro, 2017). Findings from the present study suggest that efforts should be made to continue with prevention strategies around awareness of drug use during adolescence and adverse consequences, e.g. psychotic-like experiences; particularly when considering that in some cases subclinical psychotic-like experiences can be associated with a later clinical diagnosis of psychotic illness. A study conducted in the Netherlands found that, psychotic-like experiences when combined with environmental exposures, can result in abnormal persistence of psychotic-like experiences (Cougnard et al., 2007).

7.7. Implications for Future Research

Findings from the present study have demonstrated a gap in knowledge regarding cannabis use and psychotic-like experiences in adolescents, particularly around type of cannabis used and potency. Research assessing levels of THC in cannabis and psychotic-like experiences has continuously found (Di Forti et al., 2015; Di Forti et al., 2009; Di Forti et al., 2019; Di Forti et al., 2014; Morgan & Curran, 2008; Morgan et al., 2012) that high-potency cannabis use increases the risk for psychosis. However, studies

that have been conducted in adolescents have not assessed type of cannabis used until now. It is relevant to determine if the association found in adults between high-potency cannabis use and psychotic-like experiences replicates in adolescent population, particularly with the increase of cannabis legalisation, for medicinal and recreational use (Hall et al., 2019).

This is the first study conducted in Mexico that examined the association between cannabis use and psychotic-like experiences. Furthermore, it is the first one to assess type of cannabis used. This highlighted the importance of conducting further research as there is little understanding and education around cannabis. When conducting data collection, one particular thing that drew my attention was that, even when adolescents did know about different types of cannabis, most of the adult population, who supported me during data collection, did not. Most of them were clinicians working in substance misuse treatment services and teachers in middle schools. Moreover, it was not a factor to be considered when entering treatment, in the case of the substance misuse clinical sample. Cannabis was simply identified as cannabis, without regard of potency and how this could be impacting the adolescent's mental health.

Most research conducted in Mexico in substance use has been of epidemiological nature and, unfortunately results are limited to publications in government reports (Villatoro et al., 2012). There is not wide dissemination of scientific research, and unless there is a particular interest in the topic, data is hardly disseminated to the general population. More research has to be conducted around substance use and, particularly in mental health. During the development of this study I continuously searched for publications

addressing mental health in adolescents in Mexico and nothing was found. Not even government document that stated prevalence of mental health problems in adults or adolescents.

As show in Chapter 1, there is an increasing prevalence of cannabis use among the adolescent population and is important to understand the effects of cannabis use in Mexican population. Research around prevalence of cannabis use is not sufficient, there is an urgent need for updated knowledge around substance use and mental health, which unfortunately, is not a priority. Despite substance use being a matter of public health concern in the country, there has not been much research conducted in Mexico. Undoubtedly, it is more a matter of lack of funding from the government to research, than a lack of interest from researchers in the country. Further exploration on the association between cannabis use and psychotic-like experiences in suggested. However, a longitudinal design may be more informative of the association alongside assessment of mental health problems. A more comprehensive assessment of psychopathology, childhood trauma and family history of mental health problems. Assessment at different time points alongside biological measures.

7.8. Public Health and Policy Implications

7.8.1. Public Health: Prevention

Findings show cannabis use among the adolescent student sample is significantly associated with use of other drugs, and that, similarly, psychotic-like experiences are significantly associated with use of other drugs. Overall, age of onset of cannabis use is prior to onset of use of illicit drugs, and the use of cannabis might be a risk factor for

the onset of use of other drugs. As previously mentioned, illicit drug use is linked with psychotic-like experiences, therefore, it is important to design prevention strategies to reduce use of illicit drugs in the adolescent population. However, prevention should come from early stages, and education around drug use might help, however, research has shown that there are other factors that may have a more significant impact in preventing drug use (Wills, Ainette, Stoolmiller, Gibbons, & Shinar, 2008) for example, an enhanced ability to solve problems and planned ahead. Cannabis use might not represent a feasible target for psychosis prevention by itself. As previously discussed, psychosis is an illness with no determined ethology. There are a number of risk factors that could influence the development of psychosis. A successful prevention strategy should include different targets rather than just a specific one, in this case cannabis and other drug use.

For example, the Icelandic Model of Adolescent Substance Use Prevention is one of the most effective programmes in place, it has been developed from an evidence based perspective and it comprises a much broader scope than only substance use education, e.g. family and community involvement (Sigfúsdóttir, Thorlindsson, Kristjánsson, Roe, & Allegrante, 2009). Prevalence of daily tobacco use, past month alcohol and lifetime use of hashish declined almost 50% in 10 after the implementation of the prevention programme (Sigfusdottir, Kristjansson, Thorlindsson, & Allegrante, 2008).

There are strategies in place reported by the government in Mexico and, from what it has been found, it is a priority that is being addressed from the start of the new government (Sanchez Guerrero, 2019). These strategies intend to standardize actions

conducted by all different federal entities and councils. However, the government report cited was published in 2019, before it was made public the intention to pass a legislation to regulate cannabis and there is nothing regarding this matter in the document (Sanchez Guerrero, 2019).

7.8.2. Policy Implications

In January 2020 the Mexican Senate informed that a new legislation to legalise and regulate cannabis in the country will take effect. Debates around legalising cannabis started in 2016, but this is the first time an end date has been announced, being April of 2020 the date it will be decided the effect of the law (Republica, 2020). The official document states that main intention of this law is to legally regulate use, cultivation, distribution, exportation, possession, and transportation, promote scientific research, among many others (Republica, 2020). The government, through the creation of a Mexican Cannabis Institute will regulate cannabis and every matter related to it, for example limits around potency. Levels have not yet been mentioned in the document; however, it states that any product that exceeds the proposed limit stated by the institute will be prohibited.

Results from the present study show that cannabis use is associated with lifetime use of other drugs in the student sample, particularly with illicit drugs; and, in the substance misuse clinical sample, daily cannabis use was significantly associated with frequent use of methamphetamines. These results, alongside age of onset of cannabis and illicit drugs reported by participants, suggest that cannabis use may be a risk factor for use of other drugs in adolescence. Now that this legislation is in place, it would be advised that

the government stablish effective and consistent substance use prevention programmes across the country (Faggiano, Minozzi, Versino, & Buscemi, 2014). Moreover, to set these programmes particularly from an early age, as research has shown that prevention at an early age is better than later in life (Lubman, Hides, Yücel, & Toumbourou, 2007). Furthermore, public policies should be encouraged to prevent increase of use, for example taxation (Hall et al., 2019).

Several states in the US have legalised recreational cannabis, with Washington and Colorado being the first ones in 2012 (Hall & Lynskey, 2016). Recently, results from the Washington Health Youth Survey were publishes, comparing their results with results from the Monitoring the Future National Survey Results on Drug Use (Johnston, 2018). The later had reported an increase in cannabis use among adolescents; however researchers from the Washington Health Youth Survey reported a decrease in cannabis use in that particular state (Dilley et al., 2019). It still difficult to assess if legalisation has had an impact on use (Leung, Chiu, Stjepanović, & Hall, 2018), however, there are some important critics around how cannabis has been regulated in the US, e.g. there is no clear regulation on promotion, availability and taxation on high-potency products (Hall & Lynskey, 2016). These concerns should be taken into account now that cannabis is to be legal in Mexico, and the government should regulate it does not happen.

Canada legalised cannabis in 2018, making it the second country in legalising cannabis for recreational use, with Uruguay being the first in 2013 (Faccio, 2019). However,

contrary to what has been seen in the US, Canada's implementation seems much more focused on minimizing harms related with legalisation.

The National Council against Addictions in Mexico (CONADIC) is responsible of overlooking substance misuse problems in the country and in charge of designing and set different strategies in the matter. However, during the time this study was conducted, when data were collected and during the time I have had the chance of working in the addictions field in Mexico, there are not enough resources given to institutions to deal with substance use; not for prevention strategies and not for treatment services.

In the clinical sample results show a strong association between daily and heavy use of cannabis with frequent use of methamphetamines and solvents. Considering mean age of first use of cannabis and mean age of onset of solvents and methamphetamine use it can be observed that cannabis use precedes use of methamphetamines and solvents. As previously mentioned, research has shown a that cannabis is associated with use of other drugs (Hall & Lynskey, 2005), furthermore, a study analysing data from 17 countries found that initiation of drugs considered as 'gateway drugs' (tobacco, alcohol, cannabis) was associated with later onset of illicit drugs (Degenhardt et al., 2010).

The significantly high associations found between cannabis use and use of illicit drugs, particularly in the school sample is unsettling, especially when considering data from the substance misuse sample. This raises the question of how many of the students using

cannabis and other drugs will end in a substance misuse treatment service from where the clinical data was collected or other type of substance misuse treatment service. There is an urgent need of evidence-based prevention strategies and substance use treatment services.

Having cannabis legalised in Mexico could have a number of benefits, for example; regulation, access to cannabis for research purposes, taxation, which could result in increased availability of resources for prevention and intervention strategies for substance misuse problems and probably a significant decrease in drug-related violence in the country. However, there could be some difficulties in the process of legalising cannabis. For example, not having an evidenced-based regulation strategy; meaning that the government do not take into consideration what research has found regarding different types of cannabis and the risk of mental health problems among others. As previously mentioned, this can be observed in the United States of America, where there is no cap in concentrations of THC in commercial cannabis which increases the risk of adverse effects among users. Therefore, the importance of making an informed and evidenced-based decision.

7.9. Strengths and Limitations

7.9.1. Strengths

To the best of my knowledge, this is the first study conducted in Mexico which examines the association between cannabis use and psychotic-like experiences. Therefore, results are novel and add significant value to the addictions and mental health field in Mexico. Furthermore, it assesses type of cannabis used in an adolescent

sample (13-18-year olds) something that has not been assessed in previous studies around the world.

As the study was conducted in two different adolescent samples there is substantial addition to knowledge; firstly, from the perspective of prevention in the general population and from the harm reduction in treatment services for substance misuse. For both samples the minimum number of participants required to have enough statistical power was obtained. This is a significant accomplishment as data was collected from two different settings, schools and substance misuse treatment services. Time and resources invested were substantial in the process of collecting data. Furthermore, boroughs from where data was obtained were situated in very different areas in the city, which made the process difficult, but in the end, it was accomplished.

Questionnaires were selected carefully, particularly the psychotic-like experiences questionnaire. It was considered very important to use a questionnaire that had been previously validated in Mexico or in a population similar to the one in Mexico. Fortunately, thorough contacting the first author of a paper that reported validation of the PRIME Screen in an adolescent Mexican sample of the general population (Fresan et al., 2007), the questionnaire was obtained. Furthermore, there was minimum missing data in both, the student and the substance misuse clinical sample. Lastly, as previously mentioned, the systematic review conducted to identify previous research published around cannabis use and psychotic-like experiences in adolescents is an important addition of knowledge in the field, as this had not been examined before.

7.9.2. Limitations

Strengths of this work do not come without limitations. One important limitation is the cross-sectional design of the study, where sociodemographic characteristics, cannabis use, use of other drugs and the PRIME Screen Questionnaire were only assessed in one time period. Because of its cross-sectional nature, it is not possible to assume causality in the association between cannabis use and psychotic-like experiences. Furthermore, the nature of the study makes the detection of changes in psychotic-like experiences among participants impossible, for better understanding of the development on trends in cannabis use and psychotic-like experiences a longitudinal design would be more desirable.

Another limitation was the lack of biological measures to validate self-report measures of cannabis use. Self-report measures might be a source of bias for a number of reasons e.g. under report or recall bias (Althubaiti, 2016). However, previous studies have used similar formats (Di Forti et al., 2014; Freeman & Winstock, 2015; Mackie et al., Under Review). The reason for the selection of self-report measure was limited resources and difficulty in transporting biological samples from Mexico to the United Kingdom. Furthermore, not including a questionnaire on mental health symptoms e.g. SCL-90 (Derogatis, Lipman, & Covi, 1973) and trauma, as research has shown that trauma is an important risk factor for the development of psychotic-like experiences and other psychotic-spectrum disorders (Read et al., 2005). However, as time was limited, a careful and thorough selection of the questionnaires that were to be included in the study had to be made. Moreover, although the full set of questionnaires did not include assessment of mental health or trauma, considerable amount of data was collected from

each participant. This gives the opportunity to conduct further analyses, however there was limited time for data analysis prior to submission, therefore it was difficult to examine every single aspect of the data collected.

One important limitation regarding the cannabis questionnaire was the use of specific pictures to portray the type of cannabis participants reported to use. These pictures were used in the first stage of the project, during the piloting of questionnaires. Participants referred that the pictures did resembled to the type of cannabis they were meant to portray, however this might have been subjective as it is very difficult to be completely certain that the type of cannabis participants chose just by looking at the pictures was actually low-potency or high-potency. Moreover, as previously mentioned research regarding potency of cannabis in Mexico has never been done; making the research on this field more difficult.

Lastly, another limitation could be that as data from the student sample were collected in schools inside classrooms, this might have had an impact on reporting drug use and presence of psychotic-like experiences. However, during data collection students were not allowed to share their answers or look at other student's questionnaires. In the clinical sample, groups were significantly smaller, with a maximum of 5 participants completing the questionnaire at the same time.

7.10. Conclusion

Adolescent cannabis use is Mexico is a matter of concern and has been for over a decade. Currently, with recreational use about to be legal, efforts should be made to prevent youth, and prevent increase of use. Better treatment services should be provided and education around cannabis in the general population is urgent.

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9. Appendixes

9.1. Questionnaires

9.1.1. Demographic Questionnaire

Please complete the following questions.

a. Age

_____

b. Gender

Female	Male
1	2

c. Ethnicity: To which of the following do you identify the most?

Caucasian	Hispanic or Latino	African American	African Mexican	Asian	Other
1	2	3	4	5	6

d. Do you consider yourself part of an indigenous group?

Yes	No

e. How many rooms does your house have? Please do not include bathrooms, half bathrooms, hallways or courtyards.

1	2	3	4	5	6	7 or more

f. How many complete bathrooms with a shower and a W.C. are in the house for exclusive use of you and your family?

1	2	3	4 or more

g. Does your home have a functioning shower in any of the bathrooms?

Yes	No

h. Considering all the lightbulbs that you and your family use to light your house, including ceilings, walls, bed lamps or floor lamps, how many lightbulbs are there in your house?

0-5	6-10	11-15	16-20	21 or more

i. The floor in your house is predominantly soil, cement or other type of material?

Soil or cement	Other type of material

j. How many cars do your family own, excluding taxis?

0	1	2	3 or more

k. Does your home have a gas or electric stove?

Yes	No

l. Thinking about the family member that contributes the most economically in your house, which was the last year of studies she/he completed?

1. Did not study
2. Some Primary
3. Primary
4. Some Secondary School
5. Secondary School
6. Commercial Degree
7. Technical Degree
8. Some High School
9. High School
10. Some Undergraduate
11. Undergraduate
12. Diploma or Master
13. PhD

m. Do you have siblings?

Yes	No

n. How many?

1	2	3	4	5 or more

o. What place do you hold in your family?

First	Second	Third	Fourth	Other

If other, please specify:

_____

9.1.2. Cannabis Use Assessment

The following questionnaire contains several questions regarding cannabis use, please answer each question with complete honesty. Remember that all your answers are anonymous and confidential.

1. Have you ever smoked/used cannabis?

Yes	No
1	2

IF "NO" END OF QUESTIONNAIRE

2. Have you smoked/used cannabis in the previous 6 months?

Yes	No
1	2

3. How old were you when you first tried cannabis?

_____

4. Which of the following best describes the type of cannabis that you mainly use? (Please, choose only one).

1. Herbal Cannabis

2. Hydroponic/Redhead/Skunk

3. Hash/Resin

4. Don't know

5. Which of the following best describes the type of cannabis that is most available for you to use

Herbal Cannabis	Hydroponic/Redhead/Skunk	Hash/Resin
1	2	3

6. If you could choose one, which of the following would you prefer to use?

Herbal Cannabis	Hydroponic/Redhead/Skunk	Hash/Resin
1	2	3

7. How often do you use cannabis?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Only tried it once
1	2	3	4	5	6

8. Do you mainly use cannabis?

In a joint with tobacco	In a joint without tobacco	In a bong / water pipe	Eaten (cookies, brownies)	E-cigarette	Other
1	2	3	4	5	6

If other, please specify:

_____

9. How many joints do you smoke on a typical occasion?

¼ of a joint	½ a joint	One	Two	Three	Four or more
1	2	3	4	5	6

10. On average how much money per week do you usually spend on herbal cannabis?

I don't use this type of cannabis	Nothing (Others provide)	$20	$20-$50	$50-$80	$80-$100	$100-$150	$150-$200	$200+
1	2	3	4	5	6	7	8	9

*If you do not use this type of cannabis go to question 14

11. How long would the amount of herbal cannabis you buy per week (mentioned in the previous question) last you in days?

_____

1) Don't know

12. How many joints can you make with would the amount of herbal cannabis you buy per week (mentioned in the previous question)?

_____

1) Don't know

13. On average how many grams of herbal cannabis per week do you smoke/use?

Less than 1 gram	1 - 2 grams	2 - 3 grams	3 - 4 grams	4 - 5 grams	More than 5 grams	Don't know
1	2	3	4	5	6	7

14. On average how much money per week do you usually spend on hydroponic/redhead/skunk cannabis?

I don't use this type of cannabis	Nothing (Others provide)	$20	$20-$50	$50-$80	$80-$100	$100-$150	$150-$200	$200+
1	2	3	4	5	6	7	8	9

*If you do not use this type of cannabis go to question 18

15. How long would the amount of hydroponic/redhead/skunk cannabis you buy per week (mentioned in the previous question) last you in days?

_____

2) Don't know

16. How many joints can you make with would the amount of hydroponic/redhead/skunk cannabis you buy per week (mentioned in the previous question)?

_____

2) Don't know

17. On average how many grams of hydroponic/redhead/skunk cannabis per week do you smoke/use?

Less than 1 gram	1 - 2 grams	2 - 3 grams	3 - 4 grams	4 - 5 grams	More than 5 grams	Don't know
1	2	3	4	5	6	7

18. On average how much money per week do you usually spend on hash or resin?

I don't use this type of cannabis	Nothing (Others provide)	$20	$20-$50	$50-$80	$80-$100	$100-$150	$150-$200	$200+
1	2	3	4	5	6	7	8	9

*If you do not use this type of cannabis go to question 22

19. How long would the amount of hash you buy per week (mentioned in the previous question) last you in days?

_____

1) Don't know

20. How many joints can you make with the amount of hash you buy per week (mentioned in the previous question)?

_____

1) Don't know

21. On average how many grams of hash per week do you smoke/use?

Less than 1 gram	1 - 2 grams	2 - 3 grams	3 - 4 grams	4 - 5 grams	More than 5 grams	Don't know
1	2	3	4	5	6	7

22. Do you mainly use cannabis?

Alone	Socially (with friends)
1	2

23. Have you experienced any of the following effects after smoking cannabis? (Please choose only one option)

A. Feelings of paranoia or suspicious

Rarely or Never	Time to time	More often than not	Almost always
1	2	3	4

B. Hearing voices

Rarely or Never	Time to time	More often than not	Almost always
1	2	3	4

C. Feeling like I'm going crazy/mad

Rarely or Never	Time to time	More often than not	Almost always
1	2	3	4

D. Not wanting to do anything/ lack of motivation

Rarely or Never	Time to time	More often than not	Almost always
1	2	3	4

E. Difficulty in concentrating

Rarely or Never	Time to time	More often than not	Almost always
1	2	3	4

F. Not able to think clearly

Rarely or Never	Time to time	More often than not	Almost always
1	2	3	4

G. Seeing visions

Rarely or Never	Time to time	More often than not	Almost always
1	2	3	4

H. 'Other' please specify_____

9.1.3. Yale University PRIME Screen Questionnaire

Please read the following information before completing the questionnaire.
The following questionnaire is made of questions regarding your personal experiences. Some of these questions may be extremely related with some experiences you have had and other might not. Please answer all questions.

1. I think that I have felt that there are odd or unusual things going on that I can't explain.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 2. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

1.1 How old were you the first time you experienced this symptom?

_____

1.2 Did this symptom occur after using drugs?

Yes 1	No 2

1.2.1 Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

2. I think that I might be able to predict the future.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 3. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

2.1 How old were you the first time you experienced this symptom?

_____

2.2 Did this symptom occur following drug use?

Yes 1	No 2

Which drug?

_____

2.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

3. I may have felt that there could possibly be something interrupting or controlling my thoughts, feelings, or actions.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 4. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

3.1 How old were you the first time you experienced this symptom?

_____

3.2 Did this symptom occur after using drugs?

Yes 1	No 2

Which drug?

_____

1.4 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

4. I have had the experience of doing something differently because of my superstitions.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 5. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

4.1 How old were you the first time you experienced this symptom?

_____

4.2 Did this symptom occur after using drugs?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

5. I think that I may get confused at times whether something I experience or perceive may be real or may be just part of my imagination or dreams.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 6. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

5.1 How old were you the first time you experienced this symptom?

_____

5.2 Did this symptom occur after using any drug?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

6. I have thought that it might be possible that other people can read my mind, or that I can read other's minds.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 7. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

6.1 How old were you the first time you experienced this symptom?

_____

6.2 Did this symptom occur after using any drug?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

7. I wonder if people may be planning to hurt me or even may be about to hurt me.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 8. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

7.1 How old were you the first time you experienced this symptom?

_____

7.2 Did this symptom occur after using any drug?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

8. I believe that I have special natural or supernatural gifts beyond my talents and natural strengths.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 9. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

8.1 How old were you the first time you experienced this symptom?

_____

8.2 Did this symptom occur after using any drug?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

9. I think I might feel like my mind is “playing tricks” on me.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 10. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

9.1 How old were you the first time you experienced this symptom?

_____

9.2 Did this symptom occur after using any drug?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

10. I have had the experience of hearing faint or clear sounds of people or a person mumbling or talking when there is no one near me.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 11. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

10.1 How old were you the first time you experienced this symptom?

_____

10.2 Did this symptom occur after using any drug?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

11. I think that I may hear my own thoughts being said out loud.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 12. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

11.1 How old were you the first time you experienced this symptom?

_____

11.2 Did this symptom occur after using any drug?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

12. I have been concerned that I might be “going crazy”.

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 CONTINUE TO QUESTION NUMBER 13. OTHERWISE CONTINUE WITH THE FOLLOWING QUESTIONS.

12.1 How old were you the first time you experienced this symptom?

_____

12.2 Did this symptom occur after using any drug?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

13. Have you ever seen something or someone that other people could not see?

Definitely disagree 1	Somewhat disagree 2	Slightly disagree 3	Not sure 4	Slightly agree 5	Definitely agree 6

IF YOU ANSWERED DEFINITELY DISAGREE #1 END OF QUESTIONNAIRE

13.1 How old were you the first time you experienced this symptom?

_____

13.2 Did this symptom occur after using any drug?

Yes 1	No 2

Which drug?

_____

1.3 Did you ever experience this symptom without the use of any drug?

Yes 1	No 2

End of Questionnaire

9.1.4. Other Substance Use

A. Tobacco

a. Have you ever smoked tobacco?

Yes	No (Go to section B)

b. How old were you when you first smoked tobacco?

_____

c. How often do you smoke tobacco?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

B. Alcohol

a. Have you ever drunk alcohol?

Yes	No (Go to section B)

b. How old were you when you had your first sip of alcohol?

_____

c. How old were you when you had your first whole glass of alcohol?

_____

d. How often do you drink alcohol?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

e. How often have you had 4 or more if girl 5 or more if boy drinks in one occasion?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once	Never done it
1	2	3	4	5	6	7

C. Cocaine

a. Have you ever tried cocaine?

Yes	No (Go to section B)

b. How old were you when you first tried cocaine?

_____

c. How often do you use cocaine?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

D. Crack

a. Have you ever smoked crack?

Yes	No (Go to section B)

b. How old were you when you first smoked crack?

_____

c. How often do you smoke crack?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

E. Solvents

a. Have you ever tried solvents?

Yes	No (Go to section B)

b. How old were you when you first tried solvents?

_____

c. How often do you use solvents?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

F. Hallucinogens

a. Have you ever tried hallucinogens?

Yes	No (Go to section B)

b. How old were you when you first tried hallucinogens?

_____

c. How often do you use hallucinogens?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

G. Ecstasy

a. Have you ever tried ecstasy?

Yes	No (Go to section B)

b. How old were you when you first tried ecstasy?

_____

c. How often do you use ecstasy?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

H. Benzodiazepines or Sleeping Pills

a. Have you ever tried benzodiazepines or sleeping pills?

Yes	No (Go to section B)

b. How old were you when you first tried benzodiazepines or sleeping pills?

_____

c. How often do you use benzodiazepines or sleeping pills?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

I. Opioids

a. Have you ever tried opioids?

Yes	No (Go to section B)

b. How old were you when you first tried opioids?

_____

c. How often do you use opioids?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

J. Heroin or Opium

a. Have you ever tried heroin or opium?

Yes	No (Go to section B)

b. How old were you when you first tried heroin or opium?

_____

c. How often do you use heroin or opium?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

K. Relevin

a. Have you ever tried relevin?

Yes	No (Go to section B)

b. How old were you when you first tried relevin?

_____

c. How often do you use relevin?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

L. Amphetamines or Methamphetamines

a. Have you ever tried amphetamines or methamphetamines?

Yes	No (Go to section B)

b. How old were you when you first tried amphetamines or methamphetamines?

_____

c. How often do you use amphetamines or methamphetamines?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

M. Other Drugs

a. Have you ever tried any other drug that was not mentioned before?

Yes	No (Go to section B)

b. Which?

_____

c. How old were you when you first tried this drug?

_____

d. How often do you use this drug?

Every day or almost daily	Once or twice a week	Once or twice a month	Less than once a month	Once or twice a year	Just tried it once
1	2	3	4	5	6

End of Questionnaire

9.1.5. Cuestionario Demográfico

Por favor completa las siguientes preguntas.

1. Edad (años cumplidos)

2. Sexo

Femenino	Masculino
1	2

3. Etnicidad: ¿Con cuál de los siguientes grupos te identificas más?

Caucásico	Hispano o Latino	Afro-Americano	Afro- Mexicano	Asiático	Otro
1	2	3	4	5	6

4. ¿Te consideras parte de algún grupo indígena?

Si	No
1	2

5. ¿Cuál es el total de cuartos, piezas o habitaciones con que cuenta tu hogar? Por favor no incluyas baños, medio baños, pasillos, patios y zotehuelas.

1	2	3	4	5	6	7 o más

6. ¿Cuántos baños completos con regadera y W.C. (excusado) hay para uso exclusivo de los integrantes de tu hogar?

1	2	3	4 o más

7. ¿En tu hogar cuentas con regadera funcionando en alguno de los baños?

Si	No
1	2

8. Contando todos los focos que se utilizan para iluminar tu hogar, incluyendo los de techos, paredes y lámparas de buro o piso, ¿cuántos focos tiene tu hogar?

0 – 5	6 – 10	11 – 15	16 – 20	21 o más
1	2	3	4	5

9. ¿El piso de tu hogar es predominantemente de tierra, cemento o de algún otro tipo de acabado?

Tierra o cemento	Otro tipo de material o acabado
1	2

10. ¿Cuántos automóviles propios, excluyendo taxis, tienen en tu hogar?

0	1	2	3 o más

11. ¿En tu hogar cuentan con estufa de gas o eléctrica?

Si	No
1	2

12. Pensando en la persona que aporta la mayor parte del ingreso económico a tu hogar, ¿cuál fue el último año de estudios que él o ella completó?

1. No estudió
2. Primaria incompleta
3. Primaria completa
4. Secundaria incompleta
5. Secundaria completa
6. Carrera comercial

7. Carrera técnica
8.Preparatoria incompleta
9. Preparatoria completa
10. Licenciatura incompleta
11. Licenciatura completa
12. Diplomado o Maestría
13. Doctorado

13. ¿Tienes hermanos?

Si 1	No 2

14. ¿Cuántos?

1	2	3	4	5 o mas

15. ¿Qué lugar ocupas en tu familia?

Primer hijo 1	Segundo hijo 2	Tercero hijo 3	Cuarto hijo 4	Otro 5

Si tu respuesta fue otro, por favor especifica:

FIN DEL PRIMER CUESTIONARIO

9.1.6. Cuestionario De Uso De Marihuana

El siguiente cuestionario contiene preguntas acerca del uso de marihuana, por favor responde cada pregunta honestamente. Recuerda que tus respuestas son anónimas y confidenciales.

1. ¿Alguna vez has fumado o usado marihuana?

Si	No*
1	2

***SÍ TU RESPUESTA FUE "NO", FIN DE ESTE CUESTIONARIO, POR FAVOR CONTINUA CON EL SIGUIENTE CUESTIONARIO**

2. ¿Has fumado o utilizado marihuana en los últimos 6 meses?

Si	No
1	2

3. ¿Qué edad tenías la primera vez que probaste la marihuana?

4. ¿Cuál de las siguientes imágenes representa mejor el tipo de marihuana que utilizas con mayor frecuencia? **POR FAVOR ESCOGE SÓLO UNA OPCIÓN.**



5. ¿Cuál de las siguientes opciones es el tipo de marihuana que te es más fácil conseguir?

Marihuana herbal	Hidropónica, Pelirroja, Skunk	Hash o Resina
1	2	3

6. De las siguientes opciones, ¿Cuál es el tipo de marihuana que prefieres consumir?

Marihuana herbal	Hidropónica, Pelirroja, Skunk	Hash o Resina
1	2	3

7. ¿Qué tan seguido consumes marihuana?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez al mes	Una o dos veces al año	Solo consumí una vez
1	2	3	4	5	6

8. Generalmente, ¿De qué forma consumes marihuana?

En un cigarro con tabaco	En un cigarro sin tabaco	En bong o pipa	En comida (brownies, etc.)	En cigarro electrónico	Otra (especifica)
1	2	3	4	5	6

*Si tu respuesta fue "Otra" por favor especifica:

9. Cuando consumes marihuana, aproximadamente, ¿Cuántos cigarros consumes?

¼ de Cigarro	1/2 Cigarro	Uno	Dos	Tres	Cuatro o Más
1	2	3	4	5	6

10. En promedio, ¿Cuánto dinero gastas a la semana en marihuana herbal?

No consumo marihuana herbal*	Nada (Te regalan o amigos compran)	$20	$20-$50	$50-$80	$80-$100	$100-$150	$150-$200	Más de $200
1	2	3	4	5	6	7	8	9

***SI NO CONSUMES ESTE TIPO DE MARIHUANA, POR FAVOR PASA A LA PREGUNTA #14.**

11. Aproximadamente, la cantidad de marihuana herbal que compras por semana, ¿Cuántos días te dura? (Cantidad mencionada en la pregunta anterior).

1) No lo sé

12. ¿Cuántos cigarros puedes hacer con la cantidad de marihuana herbal que compras por semana? (Cantidad mencionada en la pregunta 10).

1) No lo sé

13. En promedio, ¿Cuántos gramos de marihuana herbal consumes por semana?

Menos de 1 gramo	1 - 2 gramos	2 - 3 gramos	3 - 4 gramos	4 - 5 gramos	Más de 5 gramos	No sé
1	2	3	4	5	6	7

14. En promedio, ¿Cuánto dinero gastas a la semana en marihuana hidropónica, pelirroja o skunk?

No consumo este tipo de marihuana*	Nada (Te regalan o amigos compran)	$20	$20-$50	$50-$80	$80-$100	$100-$150	$150-$200	Más de $200
1	2	3	4	5	6	7	8	9

***SI NO CONSUMES ESTE TIPO DE MARIHUANA, POR FAVOR PASA A LA PREGUNTA #18.**

15. Aproximadamente, la cantidad de marihuana hidropónica, pelirroja o skunk que compras por semana, ¿Cuántos días te dura? (Cantidad mencionada en la pregunta anterior).

1) No lo sé

16. ¿Cuántos cigarros puedes hacer con la cantidad de marihuana hidropónica, pelirroja o skunk que compras por semana? (Cantidad mencionada en la pregunta 14).

1) No lo sé

17. En promedio, ¿Cuántos gramos de marihuana hidropónica, pelirroja o skunk consumes por semana?

Menos de 1 gramo	1 - 2 gramos	2 - 3 gramos	3 - 4 gramos	4 - 5 gramos	Más de 5 gramos	No sé
1	2	3	4	5	6	7

18. En promedio, ¿Cuánto dinero gastas a la semana en hash?

No consumo hash*	Nada (Te regalan o amigos compran)	$20	$20-$50	$50-$80	$80-$100	$100-$150	$150-$200	Más de $200
1	2	3	4	5	6	7	8	9

***SI NO CONSUMES HASH, POR FAVOR PASA A LA PREGUNTA #22.**

19. Aproximadamente, la cantidad de hash que compras por semana, ¿Cuántos días te dura? (Cantidad mencionada en la pregunta anterior).

2) No lo sé

20. ¿Cuántos cigarros puedes hacer con la cantidad de hash que compras por semana? (Cantidad mencionada en la pregunta 18).

2) No lo sé

21. En promedio, ¿Cuántos gramos de hash consumes a la semana?

Menos de 1 gramo	1 - 2 gramos	2 - 3 gramos	3 - 4 gramos	4 - 5 gramos	Más de 5 gramos	No sé
1	2	3	4	5	6	7

22. Principalmente consumes marihuana:

Solo/Sola	Socialmente (con amigos)
1	2

23. ¿Alguna vez has experimentado alguno de los siguientes síntomas <u>después de consumir marihuana?</u> (Por favor elige sólo una opción).

I. Paranoia o suspicacia

Raramente o Nunca	A veces	Seguido	Casi siempre
1	2	3	4

J. Escuchar voces

Raramente o Nunca	A veces	Seguido	Casi siempre
1	2	3	4

K. Sentir que te estas volviendo loco / loca

Raramente o Nunca	A veces	Seguido	Casi siempre
1	2	3	4

L. Sin ganas o sin motivación

Raramente o Nunca	A veces	Seguido	Casi siempre
1	2	3	4

M. Dificultad para concentrarte

Raramente o Nunca	A veces	Seguido	Casi siempre
1	2	3	4

N. No pensar claramente

Raramente o Nunca	A veces	Seguido	Casi siempre
1	2	3	4

O. Ver visiones (ver cosas de forma alterada pero que si están ahí)

Raramente o Nunca	A veces	Seguido	Casi siempre
1	2	3	4

P. Otras, por favor especifica

FIN DEL TERCER CUESTIONARIO

9.1.7. Tamizaje De Síntomas Prodrómicos PRIME

El siguiente cuestionario hace preguntas acerca de tu experiencia personal. Preguntamos acerca de algunas experiencias sensoriales, psicológicas, emocionales y sociales. Algunas de estas preguntas pueden estar muy relacionadas con experiencias que has vivido y otras no. Por favor contesta TODAS las preguntas.

1. Creo que pasan cosas raras o inusuales que no puedo explicar.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 2. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

1.5 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

1.6 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

1.2.1 ¿Qué droga?

_____

1.7 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

2. Creo que soy capaz de predecir el futuro.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 3. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

2.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

2.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

2.2.1 ¿Qué droga?

_____

2.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

3. He sentido que hay algo que interrumpe o controla mis pensamientos, sentimientos o acciones.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 4. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

3.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

3.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

3.2.1 ¿Qué droga?

_____

3.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

4. He tenido la experiencia de hacer cosas de forma distinta a los demás debido a mis supersticiones.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 5. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

4.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

4.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

4.2.1 ¿Qué droga?

_____

4.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

5. En algunas ocasiones me he confundido al no saber si algo que vivo o percibo es real o solo es parte de mi imaginación.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 6. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

5.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

5.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

5.2.1 ¿Qué droga?

_____

5.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

6. Es posible que otras personas puedan leer mi mente o yo puedo leer la mente de los demás.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 7. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

6.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

6.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

6.2.1 ¿Qué droga?

_____

6.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

7. Me pregunto si la gente planea hacerme daño o si va a hacerme daño.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 8. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

7.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

7.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

7.2.1 ¿Qué droga?

_____

7.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

8. Creo que tengo poderes especiales o sobrenaturales, además de mis propios talentos.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 9. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

8.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

8.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

8.2.1 ¿Qué droga?

_____

8.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

9. A veces creo que mi mente "me juega trucos o me engaña".

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 10. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

9.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

9.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

9.2.1 ¿Qué droga?

_____

9.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

10. He tenido la experiencia de escuchar cosas o la voz de una persona(s) susurrándome o hablándome cuando no hay nadie cerca de mí.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 11. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

10.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

10.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

10.2.1 ¿Qué droga?

_____

10.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

11. Creo que he escuchado mis propios pensamientos en voz alta.

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 12. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

11.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

11.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:
11.2.1 ¿Qué droga?

_____

11.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

12. Me preocupa que me esté "volviendo loco".

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" PASA A LA PREGUNTA 13. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

12.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

12.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

12.2.1 ¿Qué droga?

_____

12.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

13. ¿Alguna vez has visto algo o a alguien que otras personas no podían ver?

Totalmente en desacuerdo	En desacuerdo	Un poco en desacuerdo	No estoy seguro	Un poco de acuerdo	Totalmente de acuerdo
1	2	3	4	5	6

SÍ RESPONDISTE "TOTALMENTE EN DESACUERDO" FIN DEL CUESTIONARIO. DE LO CONTRARIO CONTINUA CON LAS SIGUIENTES PREGUNTAS.

13.1 ¿Qué edad tenías la primera vez que experimentaste esto?

_____

13.2 ¿Cuándo experimentaste esto, ocurrió bajo los efectos de alguna droga?

Si	No
1	2

Sí tu respuesta fue si, por favor especifica:

13.2.1 ¿Qué droga?

_____

13.3 ¿Alguna vez experimentaste este síntoma **sin** el uso de alguna sustancia?

Si	No
1	2

Consumo de Otras Drogas

A. TABACO

a. ¿Alguna vez has consumido tabaco?

Si	No
1	(Pasa a la sección B) 2

a. ¿Qué edad tenías la primera vez que probaste el tabaco?

_____

b. ¿Con qué frecuencia consumes tabaco?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo probé una vez
1	2	3	4	5	6

B. ALCOHOL

a. ¿Alguna vez has consumido alcohol?

Si	No
1	(Pasa a la sección C) 2

b. ¿Qué edad tenías la primera vez que probaste el alcohol?

_____

c. ¿Qué edad tenías la primera vez que tomaste una copa de alcohol?

_____

d. ¿Con qué frecuencia consumes alcohol?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo probé una vez
1	2	3	4	5	6

e. ¿Con qué frecuencia consumes más de 4 copas de alcohol por ocasión si eres mujer o más de 5 copas de alcohol si eres hombre?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo hice una vez	Nunca lo he hecho
1	2	3	4	5	6	7

C. COCAÍNA EN POLVO

d. ¿Alguna vez has consumido cocaína en polvo?

Si	No
1	(Pasa a la sección D) 2

e. ¿Qué edad tenías la primera vez que consumiste cocaína en polvo?

_____

f. ¿Con qué frecuencia consumes cocaína en polvo?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo la probé una vez
1	2	3	4	5	6

D. COCAÍNA BASE, CRACK O PIEDRA

d. ¿Alguna vez has consumido cocaína base, crack o piedra?

Si	No
1	(Pasa a la sección E) 2

e. ¿Qué edad tenías la primera vez que consumiste cocaína base, crack o piedra?

_____

f. ¿Con qué frecuencia consumes cocaína base, crack o piedra?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo probé una vez
1	2	3	4	5	6

E. INHALABLES O SOLVENTES

d. ¿Alguna vez has consumido inhalables o solventes?

Si	No
1	(Pasa a la sección F) 2

e. ¿Qué edad tenías la primera vez que consumiste inhalables o solventes?

_____

f. ¿Con qué frecuencia consumes inhalables o solventes?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo probé una vez
1	2	3	4	5	6

F. ALUCINÓGENOS

d. ¿Alguna vez has consumido alucinógenos?

Si	No
1	(Pasa a la sección G) 2

e. ¿Qué edad tenías la primera vez que consumiste alucinógenos?

_____

f. ¿Con que frecuencia consumes alucinógenos?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo los probé una vez
1	2	3	4	5	6

G. ÉXTASIS

d. ¿Alguna vez has consumido éxtasis?

Si	No
1	(Pasa a la sección H) 2

e. ¿Qué edad tenías la primera vez que consumiste éxtasis?

_____

f. ¿Con qué frecuencia consumes éxtasis?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo probé una vez
1	2	3	4	5	6

H. TRANQUILIZANTES O PASTILLAS PARA DORMIR

d. ¿Alguna vez has consumido tranquilizantes o pastillas para dormir?

Si	No
1	(Pasa a la sección I) 2

e. ¿Qué edad tenías la primera vez que consumiste tranquilizantes o pastillas para dormir?

_____

f. ¿Con qué frecuencia consumes tranquilizantes o pastillas para dormir?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo las probé una vez
1	2	3	4	5	6

I. OPIÁCEOS

d. ¿Alguna vez has consumido opiáceos?

Si	No
1	(Pasa a la sección J) 2

e. ¿Qué edad tenías la primera vez que consumiste opiáceos?

_____

f. ¿Con qué frecuencia consumes opiáceos?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo probé una vez
1	2	3	4	5	6

J. HEROÍNA U OPIO

d. ¿Alguna vez has consumido heroína u opio?

Si	No
1	(Pasa a la sección K) 2

e. ¿Qué edad tenías la primera vez que consumiste heroína u opio?

_____

f. ¿Con qué frecuencia consumes heroína u opio?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo probé una vez
1	2	3	4	5	6

K. RELEVIN

d. ¿Alguna vez has consumido relevin?

Si	No
1	(Pasa a la sección L) 2

e. ¿Qué edad tenías la primera vez que consumiste relevin?

_____

f. ¿Con qué frecuencia consumes relevin?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo probé una vez
1	2	3	4	5	6

L. ANFETAMINAS O METANFETAMINAS

d. ¿Alguna vez has consumido anfetaminas o metanfetaminas?

Si	No
1	(Pasa a la sección M) 2

e. ¿Qué edad tenías la primera vez que consumiste anfetaminas o metanfetaminas?

_____

f. ¿Con qué frecuencia consumes anfetaminas o metanfetaminas?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo lo probé una vez
1	2	3	4	5	6

M. CIGARROS ELECTRÓNICOS

a. ¿Alguna vez has consumido cigarros electrónicos?

Si	No
1	(Pasa a la sección N) 2

b. ¿Qué edad tenías la primera vez que consumiste cigarros electrónicos?

_____

c. ¿Con que frecuencia consumes cigarros electrónicos?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo los probé una vez
1	2	3	4	5	6

N. OTRAS DROGAS

a. ¿Alguna vez has consumido alguna otra droga que no se haya mencionado anteriormente?

Si	No
1	(Fin del Cuestionario) 2

b. ¿Cuál?

_____

c. ¿Qué edad tenías la primera vez que consumiste esta droga?

_____

d. ¿Con qué frecuencia consumes esta droga?

Todos los días o casi todos los días	Una o dos veces por semana	Una o dos veces por mes	Menos de una vez por mes	Una o dos veces al año	Solo la probé una vez
1	2	3	4	5	6

FIN DEL CUESTIONARIO

9.2. Systematic Review: Search Strategies

9.2.1. ASSIA Applied Social Sciences Index and Abstracts

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse

   Drug abuse

2. Cannabis

   Skunk

3. Marijuana
4. Cannabis use
5. Adolescent

   Adolescent psychiatry

6. Psychotic symptom* / Psychotic N/5 symptom*
7. Psychosis
8. Prodrom* N/5 symptom*
9. Vulnerability N/5 psychosis
10. Early onset N/5 psychosis
11. First episode N/5 psychosis
12. Psychotic like N/5 experiences

Defined Search Strategy: Systematic Review

((“substance abuse”) OR (“drug abuse”) OR (cannabis) OR (skunk) OR (marijuana) OR (“cannabis use”)) AND ((adolescent) OR (“adolescent psychiatry”)) AND ((“psychotic symptom*”) OR (psychotic N/5 symptom) OR (psychosis) OR (prodrom* N/5

symptom*) OR (vulnerability N/5 psychosis) OR ("early onset" N/5 psychosis) OR ("first episode" N/5 psychosis) OR ("psychotic like" N/5 experiences))

((substance abuse) OR (drug abuse) OR (cannabis) OR (skunk) OR (marijuana) OR (cannabis use)) AND ((adolescent) OR (adolescent psychiatry)) AND ((psychotic symptom*) OR (psychotic N/5 symptom) OR (psychosis) OR (prodrom* N/5 symptom*) OR (vulnerability N/5 psychosis) OR (early onset N/5 psychosis) OR (first episode N/5 psychosis) OR (psychotic like N/5 experiences))

Total: 51

Literature Review: Cannabis Use in Mexico

1. Substance abuse

   Drug abuse

2. Addiction

   Drug addiction

3. Cannabis / Marijuana / Marihuana

   Skunk

4. Cannabis use
5. Mexico

Defined Search Strategy: Literature Review Mexico

(("substance abuse") OR ("drug abuse") OR (addiction) OR ("drug addiction") OR (cannabis) OR (marijuana) OR (marihuana) OR (skunk) OR ("cannabis use")) AND ((Mexico))

((substance abuse) OR (drug abuse) OR (addiction) OR (drug addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (skunk) OR (cannabis use)) AND ((Mexico))

Total: 176

9.2.2. CINHAL: Cumulative Index to Nursing and Allied Health Literature

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse
2. Cannabis
3. Marijuana
4. Cannabis use
5. Adolescent

   Adolescent psychiatry

6. Psychotic symptom*
7. Psychosis
8. Prodrom* symptom*
9. Vulnerability for psychosis

   Substance-induced psychoses

10. Early onset psychosis
11. First episode psychosis
12. Psychotic like experiences

Defined Search Strategy: Systematic Review

((“substance abuse”) OR (cannabis) OR (marijuana) OR (“cannabis use”)) AND (adolescent) OR (“adolescent psychiatry”)) AND ((“psychotic symptom*”) OR

(psychosis) OR (“prodrom* symptom*”) OR (“vulnerability for psychosis”) OR (“substance-induced psychoses”) OR (“early onset psychosis”) OR (“first episode psychosis”) OR (“psychotic like experiences”))

((substance abuse) OR (cannabis) OR (marijuana) OR (cannabis use)) AND (adolescent) OR (adolescent psychiatry)) AND ((psychotic symptom*) OR (psychosis) OR (prodrom* symptom*) OR (vulnerability for psychosis) OR (substance-induced psychoses) OR (early onset psychosis) OR (first episode psychosis) OR (psychotic like experiences))

Total: 3,896

Literature Review: Cannabis Use in Mexico

1. Substance abuse
2. Addiction

   Substance dependence

3. Cannabis / Marijuana / Marihuana
4. Cannabis use
5. Mexico

Defined Search Strategy: Literature Review Mexico

((“substance abuse”) OR (addiction) OR (“substance dependence”) OR (cannabis) OR (marijuana) OR (marihuana) OR (“cannabis use”)) AND ((Mexico))

((substance abuse) OR (addiction) OR (substance dependence) OR (cannabis) OR (marijuana) OR (marihuana) OR (cannabis use)) AND ((Mexico))

Total: 266

9.2.3. Cochrane

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse

   Substance related disorders

2. Cannabis

   Marijuana abuse

   Marijuana smoking

3. Marijuana
4. Cannabis use

   Cannabis abuse

5. Adolescent

   Adolescent psychiatry

   Adolescent psychology

6. Psychotic symptom* / Psychotic near Symptom*
7. Psychosis

   Substance induced psychoses

8. Prodrom* symptom* / Prodrom* near Symptom*
9. Vulnerability for psychosis / Vulnerability near Psychosis
10. Early onset psychosis / “Early onset” near Psychosis
11. First episode psychosis / “First episode” near Psychosis
12. Psychotic like experiences / “Psychotic like” near Experiences

Defined Search Strategy: Systematic Review

((“substance abuse”) OR (“substance related disorders”) OR (cannabis) OR (“marijuana abuse”) OR (“marijuana smoking”) OR (marijuana) OR (“cannabis use”) OR (“cannabis abuse”)) AND ((adolescent) OR (“adolescent psychiatry”)) AND ((“psychotic symptom*”) OR (psychosis) OR (“substance induced psychoses”) OR (“prodrom* symptom*”) OR (prodrom* near symptom*) OR (“vulnerability for psychosis”) OR (vulnerability near psychosis) OR (“early onset psychosis”) OR (“early onset” near psychosis) OR (“first episode psychosis”) OR (“first episode” near psychosis) OR (“psychotic like experiences”) OR (“psychotic like” near experiences))

((substance abuse) OR (substance related disorders) OR (cannabis) OR (marijuana abuse) OR (marijuana smoking) OR (marijuana) OR (cannabis use) OR (cannabis abuse)) AND ((adolescent) OR (adolescent psychiatry)) AND ((psychotic symptom*) OR (psychosis) OR (substance induced psychoses) OR (prodrom* symptom*) OR (prodrom* near symptom*) OR (vulnerability for psychosis) OR (vulnerability near psychosis) OR (early onset psychosis) OR (early onset near psychosis) OR (first episode psychosis) OR (first episode near psychosis) OR (psychotic like experiences) OR (psychotic like near experiences))

Total: 57

Literature Review: Cannabis Use in Mexico

1. Substance abuse

   Substance related disorders

2. Addiction
3. Cannabis / Marijuana / Marihuana

Marijuana abuse

Marijuana smoking

4. Cannabis use

   Cannabis abuse

5. Mexico

Defined Search Strategy: Literature Review Mexico

((“substance abuse”) OR (“substance related disorders”) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (“marijuana abuse”) OR (“marijuana smoking”) OR (“cannabis use”) OR (“cannabis abuse”)) AND ((Mexico))

((substance abuse) OR (substance related disorders) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (marijuana abuse) OR (marijuana smoking) OR (cannabis use) OR (cannabis abuse)) AND ((Mexico))

Total: 21

9.2.4. EMBASE

9.2.5. Excerpta Medica Database

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse

   Drug abuse

2. Cannabis

   Cannabis addiction

   Cannabis-induced psychosis

   Cannabis smoking

3. Marijuana
4. Cannabis use

   Tetrahydrocannabinol

5. Adolescent
6. Psychotic symptom* / Psychotic ADJ5 Symptom*
7. Psychosis

   Cannabis-induced psychosis

8. Prodrom* symptom* / Prodrom* ADJ5 Symptom*
9. Vulnerability for psychosis / Vulnerability ADJ5 Psychosis

   Disease predisposition

10. Early onset psychosis / Early ADJ5 Psychosis
11. First episode psychosis / First ADJ5 Psychosis
12. Psychotic like experiences / Psychotic ADJ5 Experiences

Defined Search Strategy: Systematic Review

((“substance abuse”) OR (“drug abuse”) OR (cannabis) OR (“cannabis addiction”) OR (“cannabis-induced psychosis”) OR (“cannabis smoking”) OR (marijuana) OR (“cannabis use”) OR (tetrahydrocannabinol)) AND ((adolescent)) AND ((“psychotic symptom*”) OR (psychotic ADJ5 symptom*) OR (psychosis) OR (“prodrom* symptom*”) OR (prodrom* ADJ5 symptom*) OR (“vulnerability for psychosis”) OR (vulnerability ADJ5 psychosis) OR (“disease predisposition”) OR (“early onset psychosis”) OR (early ADJ5 psychosis) OR (“first episode psychosis”) OR (first ADJ5 psychosis) OR (“psychotic like experiences”) OR (psychotic ADJ5 experiences))

((substance abuse) OR (drug abuse) OR (cannabis) OR (cannabis addiction) OR (cannabis-induced psychosis) OR (cannabis smoking) OR (marijuana) OR (cannabis use) OR (tetrahydrocannabinol)) AND ((adolescent)) AND ((psychotic symptom*) OR (psychotic ADJ5 symptom*) OR (psychosis) OR (prodrom* symptom*) OR (prodrom* ADJ5 symptom*) OR (vulnerability for psychosis) OR (vulnerability ADJ5 psychosis) OR (disease predisposition) OR (early onset psychosis) OR (early ADJ5 psychosis) OR (first episode psychosis) OR (first ADJ5 psychosis) OR (psychotic like experiences) OR (psychotic ADJ5 experiences))

Total: 1,236

Literature Review: Cannabis Use in Mexico

1. Substance abuse

   Drug abuse

2. Addiction
3. Cannabis / Marijuana / Marihuana

Cannabis addiction

Cannabis-induced psychosis

Cannabis smoking

4. Cannabis use

   Tetrahydrocannabinol

5. Mexico

Defined Search Strategy: Literature Review Mexico

((“substance abuse”) OR (“drug abuse”) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (“cannabis addiction”) OR (“cannabis-induced psychosis”) OR (“cannabis smoking”) OR (“cannabis use”) OR (tetrahydrocannabinol)) AND ((Mexico))

((substance abuse) OR (drug abuse) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (cannabis addiction) OR (cannabis-induced psychosis) OR (cannabis smoking) OR (cannabis use) OR (tetrahydrocannabinol)) AND ((Mexico))

Total: 3,529

9.2.6. IPA: International Pharmaceutical Abstracts

9.2.7. No Subject Headings

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse
2. Cannabis
3. Marijuana
4. Cannabis use
5. Adolescent
6. Psychotic symptom* / Psychotic ADJ5 Symptom*
7. Psychosis
8. Prodrom* symptom* / Prodrom* ADJ5 Symptom*
9. Vulnerability for psychosis / Vulnerability ADJ5 Psychosis
10. Early onset psychosis / Early ADJ5 Psychosis
11. First episode psychosis / First ADJ5 Psychosis
12. Psychotic like experiences / Psychotic ADJ5 Experiences

Defined Search Strategy: Systematic Review

((“substance abuse”) OR (cannabis) OR (marijuana) OR (“cannabis use”)) AND ((adolescent)) AND ((“psychotic symptom*”) OR (psychotic adj5 symptom*) OR (psychosis) OR (“prodrom* symptom*”) OR (prodrom* adj5 symptom*) OR (“vulnerability for psychosis”) OR (vulnerability adj5 psychosis) OR (“early onset psychosis”) OR (early adj5 psychosis) OR (“first episode psychosis”) OR (first adj5 psychosis) OR (“psychotic like experiences”) OR (psychotic adj5 experiences))

((substance abuse) OR (cannabis) OR (marijuana) OR (cannabis use)) AND ((adolescent)) AND ((psychotic symptom*) OR (psychotic adj5 symptom*) OR (psychosis) OR (prodrom* symptom*) OR (prodrom* adj5 symptom*) OR (vulnerability for psychosis) OR (vulnerability adj5 psychosis) OR (early onset psychosis) OR (early adj5 psychosis) OR (first episode psychosis) OR (first adj5 psychosis) OR (psychotic like experiences) OR (psychotic adj5 experiences))

Total: 12

Literature Review: Cannabis Use in Mexico

1. Substance abuse
2. Addiction
3. Cannabis / Marihuana / Marijuana
4. Cannabis use
5. Mexico

Defined Search Strategy: Literature Review Mexico

((“substance abuse”) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (“cannabis use”)) AND ((Mexico))

((substance abuse) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (cannabis use)) AND ((Mexico))

Total: 820

9.2.8. MEDLINE

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse

   Substance related disorders

2. Cannabis
3. Marijuana
4. Cannabis use

   Marijuana abuse

   Cannabinoids

   Marijuana smoking

5. Adolescent

   Adolescent psychiatry

6. Psychotic symptom* / Psychotic ADJ5 Symptom*
7. Psychosis
8. Prodrom* symptom* / Prodrom* ADJ5 Symptom*
9. Vulnerability for psychosis / Vulnerability ADJ5 Psychosis

   Substance-induced psychoses

10. Early onset psychosis / Early ADJ5 Psychosis
11. First episode psychosis / First ADJ5 Psychosis
12. Psychotic like experiences / Psychotic ADJ5 Experiences

Defined Search Strategy: Systematic Review

((“substance abuse”) OR (“substance related disorders”) OR (cannabis) OR (marijuana) OR (“cannabis use”) OR (“marijuana abuse”) OR (“marijuana smoking”)) AND ((adolescent) OR (“adolescent psychiatry”)) AND ((“psychotic symptom*”) OR (psychotic adj5 symptom*) OR (psychosis) OR (“prodrom* symptom*”) OR (prodrom* adj5 symptom*) OR (“vulnerability for psychosis”) OR (vulnerability adj5 psychosis) OR (“substance-induced psychoses”) OR (“early onset psychosis”) OR (early adj5 psychosis) OR (“first episode psychosis”) OR (first adj5 psychosis) OR (“psychotic like experiences”) OR (psychotic adj5 experiences))

((substance abuse) OR (substance related disorders) OR (cannabis) OR (marijuana) OR (cannabis use) OR (marijuana abuse) OR (marijuana smoking)) AND ((adolescent) OR (adolescent psychiatry)) AND ((psychotic symptom*) OR (psychotic adj5 symptom*) OR (psychosis) OR (prodrom* symptom*) OR (prodrom* adj5 symptom*) OR (vulnerability for psychosis) OR (vulnerability adj5 psychosis) OR (substance-induced psychoses) OR (early onset psychosis) OR (early adj5 psychosis) OR (first episode psychosis) OR (first adj5 psychosis) OR (psychotic like experiences) OR (psychotic adj5 experiences))

Total: 498

Literature Review: Cannabis Use in Mexico

1. Substance abuse

   Substance related disorders

2. Addiction
3. Cannabis / Marijuana / Marihuana
4. Cannabis use

Marijuana abuse

Cannabinoids

5. Mexico

Defined Search Strategy: Literature Review Mexico

((“substance abuse”) OR (“substance related disorders”) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (“cannabis use”) OR (“marijuana abuse”) OR (cannabinoids)) AND ((Mexico))

((substance abuse) OR (substance related disorders) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (cannabis use) OR (marijuana abuse) OR (cannabinoids)) AND ((Mexico))

Total: 2,923

9.2.9. PsycINFO

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse

   Drug abuse

2. Cannabis
3. Marijuana
4. Cannabis use

   Marijuana usage

   Drug usage

5. Adolescent

   Adolescent psychiatry

   Adolescent psychopathology

6. Psychotic symptom* / Psychotic ADJ5 Symptom*
7. Psychosis
8. Prodrom* symptom* / Prodrom* ADJ5 Symptom*

   Prodrome

9. Vulnerability for psychosis / Vulnerability ADJ5 Psychosis
10. Early onset psychosis / Early ADJ5 Psychosis
11. First episode psychosis / First ADJ5 Psychosis
12. Psychotic like experiences / Psychotic ADJ5 Experiences

Defined Search Strategy: Systematic Review

((“substance abuse”) OR (“drug abuse”) OR (cannabis) OR (marijuana) OR (“cannabis use”) OR (“marijuana usage”) OR (“drug usage”)) AND ((adolescent) OR (“adolescent psychiatry”) OR (“adolescent psychopathology”)) AND ((“psychotic symptom*”) OR (psychotic adj5 symptom*) OR (psychosis) OR (“prodrom* symptom*”) OR (prodrom* adj5 symptom*) OR (prodrome) OR (“vulnerability for psychosis”) OR (vulnerability adj5 psychosis) OR (“early onset psychosis”) OR (early adj5 psychosis) OR (“first episode psychosis”) OR (first adj5 psychosis) OR (“psychotic like experiences”) OR (psychotic adj5 experiences))

((substance abuse) OR (drug abuse) OR (cannabis) OR (marijuana) OR (cannabis use) OR (marijuana usage) OR (drug usage)) AND ((adolescent) OR (adolescent psychiatry) OR (adolescent psychopathology)) AND ((psychotic symptom*) OR (psychotic adj5 symptom*) OR (psychosis) OR (prodrom* symptom*) OR (prodrom* adj5 symptom*) OR (prodrome) OR (vulnerability for psychosis) OR (vulnerability adj5 psychosis) OR (early onset psychosis) OR (early adj5 psychosis) OR (first episode psychosis) OR (first adj5 psychosis) OR (psychotic like experiences) OR (psychotic adj5 experiences))

Total: 554

Literature Review: Cannabis Use in Mexico

1. Substance abuse
2. Addiction

   Drug addiction

3. Cannabis / Marijuana / Marihuana
4. Cannabis use

   Marijuana usage

5. Mexico

Defined Search Strategy: Literature Review Mexico

((“substance abuse”) OR (addiction) OR (“drug addiction”) OR (cannabis) OR (marijuana) OR (marihuana) OR (“cannabis use”) OR (“marijuana usage”)) AND ((Mexico))

((substance abuse) OR (addiction) OR (drug addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (cannabis use) OR (marijuana usage)) AND ((Mexico))

Total: 4,276

9.2.10. PubMed

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse

   Substance related disorders

2. Cannabis

   Marijuana abuse

   Marijuana smoking

3. Marijuana
4. Cannabis use
5. Adolescent

   Adolescent psychiatry

6. Psychotic symptom*
7. Psychosis
8. Prodrom* symptom*
9. Early onset psychosis
10. First episode psychosis
11. Psychotic like experiences

Defined Search Strategy: Systematic Review

((“substance abuse”) OR (“substance related disorders”) OR (cannabis) OR (“marijuana abuse”) OR (“marijuana smoking”) OR (marijuana) OR (“cannabis use”)) AND ((adolescent) OR (“adolescent psychiatry”)) AND ((“psychotic symptom*”) OR

(psychosis) OR (prodrom* symptom*) OR (“early onset psychosis”) OR (“first episode psychosis”) OR (“psychotic like experiences”))

((substance abuse) OR (substance related disorders) OR (cannabis) OR (marijuana abuse) OR (marijuana smoking) OR (marijuana) OR (cannabis use)) AND ((adolescent) OR (adolescent psychiatry)) AND ((psychotic symptom*) OR (psychosis) OR (prodrom* symptom*) OR (early onset psychosis) OR (first episode psychosis) OR (psychotic like experiences))

Total: 1,560

Literature Review: Cannabis Use in Mexico

1. Substance abuse
2. Addiction
3. Cannabis / Marijuana / Marihuana

   Marijuana abuse

   Marijuana smoking

4. Cannabis use
5. Mexico

Defined Search Strategy: Literature Review Mexico

((“substance abuse”) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (“marijuana abuse”) OR (“marijuana smoking”) OR (“cannabis use”)) AND ((Mexico))

((substance abuse) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (marijuana abuse) OR (marijuana smoking) OR (cannabis use)) AND ((Mexico))

Total: 1,115

9.2.11. SCOPUS

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse
2. Cannabis
3. Marijuana
4. Cannabis use
5. Adolescent
6. Psychotic symptom* / Psychotic W/5 Symptom*
7. Psychosis
8. Prodrom* symptom* / Prodrom* W/5 Symptom*
9. Vulnerability for psychosis / Vulnerability W/5 Psychosis
10. Early onset psychosis / "Early onset" W/5 Psychosis
11. First episode psychosis / "First episode" W/5 Psychosis
12. Psychotic like experiences / Psychotic W/5 Experiences

9.2.12. No Subject Headings

Defined Search Strategy: Systematic Review

((“substance abuse”) OR (cannabis) OR (marijuana) OR (“cannabis use”)) AND ((adolescent)) AND ((“psychotic symptom*”) OR (psychotic W/5 symptom*) OR (psychosis) OR (“prodrom* symptom*”) OR (prodrom* W/5 symptom*) OR (“vulnerability for psychosis”) OR (vulnerability W/5 psychosis) OR (“early onset psychosis”) OR (“early onset” W/5 psychosis) OR (“first episode psychosis”) OR (“first

episode" W/5 psychosis) OR ("psychotic like experiences") OR ("psychotic like" W/5 experiences))

((substance abuse) OR (cannabis) OR (marijuana) OR (cannabis use)) AND ((adolescent)) AND ((psychotic symptom*) OR (psychotic W/5 symptom*) OR (psychosis) OR (prodrom* symptom*) OR (prodrom* W/5 symptom*) OR (vulnerability for psychosis) OR (vulnerability W/5 psychosis) OR (early onset psychosis) OR (early onset W/5 psychosis) OR (first episode psychosis) OR (first episode W/5 psychosis) OR (psychotic like experiences) OR (psychotic like W/5 experiences))

Total: 1,839

Literature Review: Cannabis Use in Mexico

1. Substance abuse
2. Addiction
3. Cannabis / Marijuana / Marihuana
4. Cannabis use
5. Mexico

Defined Search Strategy: Literature Review Mexico

(("substance abuse") OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR ("cannabis use")) AND ((Mexico))

((substance abuse) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (cannabis use)) AND ((Mexico))

Total: 1,027

9.2.13. Web of Science

9.2.14. No Subject Headings

Systematic Review: Cannabis Use and Psychosis in Adolescents

1. Substance abuse
2. Cannabis
3. Marijuana
4. Cannabis use
5. Adolescent
6. Psychotic symptom* / Psychotic NEAR/5 Symptom
7. Psychosis
8. Prodrom* symptom* / Prodrom* NEAR/5 Symptom
9. Vulnerability for psychosis / Vulnerability NEAR/5 Psychosis
10. Early onset psychosis / "Early onset" NEAR/5 Psychosis
11. First episode psychosis / "First episode" NEAR/5 Psychosis
12. Psychotic like experiences / "Psychotic NEAR/5 Experiences

Defined Search Strategy: Systematic Review

(("substance abuse") OR (cannabis) OR (marijuana) OR ("cannabis use")) AND ((adolescent)) AND (("psychotic symptom*") OR (psychotic NEAR/5 symptom*) OR (psychosis) OR ("prodrom* symptom*") OR (prodrom* NEAR/5 symptom*) OR ("vulnerability for psychosis") OR (vulnerability NEAR/5 psychosis) OR ("early onset psychosis") OR ("early onset" NEAR/5 psychosis) OR ("first episode psychosis") OR

("first episode" NEAR/5 psychosis) OR ("psychotic like experiences") OR ("psychotic like" NEAR/5 experiences))

((substance abuse) OR (cannabis) OR (marijuana) OR (cannabis use)) AND ((adolescent)) AND ((psychotic symptom*) OR (psychotic NEAR/5 symptom*) OR (psychosis) OR (prodrom* symptom*) OR (prodrom* NEAR/5 symptom*) OR (vulnerability for psychosis) OR (vulnerability NEAR/5 psychosis) OR (early onset psychosis) OR (early onset NEAR/5 psychosis) OR (first episode psychosis) OR (first episode NEAR/5 psychosis) OR (psychotic like experiences) OR (psychotic like NEAR/5 experiences))

Total: 1,447

Literature Review: Cannabis Use in Mexico

1. Substance abuse
2. Addiction
3. Cannabis / Marihuana / Marijuana
4. Cannabis use
5. Mexico

Defined Search Strategy: Literature Review Mexico

(("substance abuse") OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR ("cannabis use")) AND ((Mexico))

((substance abuse) OR (addiction) OR (cannabis) OR (marijuana) OR (marihuana) OR (cannabis use)) AND ((Mexico))

Total: 1,544

9.3. Systematic Review: Tables

9.3.1. Table 1. Studies Included in Systematic Review: Logistic Regression Analysis

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
1 **Cannabis Use in Adolescence and Risk for Adult Psychosis: Longitudinal Prospective Study** Arseneault, L. et al. (2002) New Zealand Prospective Longitudinal Cohort	**Participants** 759 Age range: 11-26 years old **Cannabis Use Assessment** Controls: Never or once Cannabis users at age 15: three times or more Cannabis users at age 18: three times or more **Psychotic-Like Experiences Assessment** Standardized interview scheduled (DSM-IV) (Symptoms and Disorder)	**Prevalence of Cannabis Use** NR **Prevalence of Psychotic-Like Experiences** NR	Use of other drugs Socioeconomic status Gender PLE's at 11 years old	Logistic Regression Multiple Linear Regression	**Association between Cannabis Use in Adolescence and Schizophreniform Disorder** (n=25; 3.3%) Model 1: Cannabis Use Only Cannabis Users by 15: OR: 4.50 (1.11 to 18.21) p = 0.035 Cannabis Users by 18: OR: 1.65 (0.65 to 4.18) p = 0.293 Model 2: Adds to Model 1 Controls for Childhood Psychotic Symptoms Weak Psychotic Symptoms at age 11: OR: 4.65 (1.84 to 11.78) p = 0.001 Strong Psychotic Symptoms at age 11: OR: 15.97 (3.38 to 75.47) p = 0.001 Cannabis Users by 15: OR: 3.12 (0.73 to 13.29) p = 0.124 Cannabis Users by 18: OR: 1.42 (0.54 to 3.74)	**Association between Cannabis Use in Adolescence and Schizophrenia Symptoms** (Scores 0-58) Model 1: Cannabis Use Only Cannabis Users by 15: b = 6.91 SE = 0.91 p = 0.001 Cannabis Users by 18: b = 1.04 SE = 0.40 p = 0.009 Model 2: Adds to Model 1 Controls for Childhood Psychotic Symptoms Weak Psychotic Symptoms at age 11: b = 0.68 SE = 0.53 p = 0.201 Strong Psychotic Symptoms at age 11: b = 5.16 SE = 1.39 p = 0.001 Cannabis Users by 15:

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					p = 0.473 Model 3: Adds to Model 1 Controls for Other Drug Use Other drug users at 15 to 18: OR: 0.30 (0.05 to 1.62) p = 0.160 Cannabis Users by 15: OR: 11.38 (1.84 to 70.45) p = 0.009 Cannabis Users by 18: OR: 1.95 (0.76 to 5.01) p = 0.167	b = 6.56 SE = 0.91 p = 0.001 Cannabis Users by 18: b = 1.03 SE = 0.39 p = 0.009 Model 3: Adds to Model 1 Controls for Other Drug Use Other drug users at 15 to 18: b = -0.3 SE = 0.69 p = 0.615 Cannabis Users by 15: b = 7.2 SE = 1.07 p = 0.001 Cannabis Users by 18: b = 1.1 SE = 0.42 p = 0.008
2 **Cannabis Dependence and Psychotic Symptoms in Young People** Fergusson, D.M. et al. (2003) New Zealand Longitudinal	**Participants** 1,053 **Cannabis Use Assessment** Composite International Diagnostic Interview (CIDI) Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) **Psychotic-Like Experiences Assessment** Items from the Symptom Checklist 90 (SCL-90) (Symptoms not Disorder)	**Prevalence of Cannabis Use** Dependence: 10% **Prevalence of Psychotic-Like Experiences**	Sociodemographic background Family functioning Parental adjustment Individual characteristics Prior psychotic symptoms and mental health Use of other drugs Major depression Anxiety disorders	**Logistic Regression** Negative binomial regression model to predict the logarithm of the psychotic symptom count from cannabis dependence at each age. Linkages between measures of cannabis dependence and psychotic symptom scores were modelled using a generalized estimating equation (GEE) approach.	Mean Psychotic Symptoms (Past Month) by Cannabis Dependence (Past 12 Months) at Age 18 and 21 At 18 Cannabis Dependence: *No:* Mean: 0.78 *Yes:* Mean: 2.89 p < 0.0001 Rate Ratio (95%) 3.7 (2.5 – 5.0) At 21 Cannabis Dependence: *No:* Mean: 0.87 *Yes:* Mean: 2.02	Estimated Association Between Cannabis Dependence and Psychotic Symptoms after Adjustment for Confounding Factors **Regression Parameter** B = 0.570 SE = 0.189 p < 0.005 Rate Ratio (95%) 1.8 (1.2 – 2.6)

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
			Affiliation with deviant peers Adverse life events Age of leaving the family home	Incidence Rate Ratio interpreted as the relative increase in the rate of psychotic symptoms for those who were cannabis dependent in comparison to those who were not.	$p < 0.0001$ Rate Ratio (95%) 2.3 (1.7 – 3.2)	
3 **Prospective Cohort Study of Cannabis Use, Predisposition for Psychosis, and Psychotic Symptoms in Young People** Henquet, C. et al. (2005) Germany Prospective Cohort	**Participants** 2,437 Age range 14 to 24 year olds **Cannabis Use Assessment** Munich-Composite International Diagnostic Interview (M-CIDI) **Psychotic-Like Experiences Assessment** Composite International Diagnostic Interview (M-CIDI) Symptom Checklist (SCL-90)	**Prevalence of Cannabis Use** Baseline: 13.1% Follow up: 14.8% **Prevalence of Psychotic-Like Experiences** At 4 year follow up at least one symptom: 17.4% Psychosis Baseline with Cannabis Use Yes: 424 No: 2,013 Psychosis Baseline Without Cannabis Use Yes: 342 No: 1,775	Use of other drugs Symptoms of depression Urbanicity Childhood trauma Age Gender Socioeconomic status Predisposition for psychosis	Logistic Regression	Association Between Any Cannabis Use at Baseline and Any Psychotic Symptom at Follow Up: OR (95%) Unadjusted OR: 1.79 (1.36 – 2.36) Adjusted (Age, sex, socioeconomic status, urbanicity, childhood trauma, predisposition for psychosis at baseline) OR: 1.69 (1.26 – 2.25) Additional Adjustment (Other drug use, tobacco and alcohol) OR: 1.67 (1.13 – 2.46) Additional Adjustment (Predisposition for psychosis at follow up and depression at baseline and follow up) OR: 1.53 (1.13 – 2.07) At Least 2 Psychotic Symptoms Adjusted OR: 2.23 (1.52 – 3.29) Associations Between Frequency of Cannabis Use at Baseline and Any Psychotic Symptoms: OR (95%)	NR

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					Unadjusted <1/Month: OR: 1.01 (0.55 – 1.86) 3–4 Times/Month: OR: 1.56 (0.91 – 2.68) 1–2 Times/Week: OR: 2.28 (1.28 – 4.09) 3-4 Times/Week: OR: 3.07 (1.49 – 6.31) Almost Daily: OR: 2.57 (1.52 – 4.34) Linear Trend: Increase in risk with one unit change in cannabis frequency OR: 1.24 (1.15 – 1.35) Adjusted (Age, sex, socioeconomic status, urbanicity, childhood trauma, predisposition for psychosis at baseline) <1/Month: OR: 0.99 (0.53 – 1.84) 3–4 Times/Month: OR: 1.50 (0.86 – 2.62) 1–2 Times/Week: OR: 1.95 (1.07 – 3.55) 3-4 Times/Week: OR: 2.44 (1.16 – 5.13) Almost Daily: OR: 2.23 (1.30 – 3.84)	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					Linear Trend: Increase in risk with one unit change in cannabis frequency OR: 1.20 (1.10 – 1.31)	
4 **Association of Cannabis Use with Prodromal Symptoms of Psychosis in Adolescence** Miettunen, J. et al. (2008) Finland Prospective Cohort	**Participants** 6,330 Age range 15 to 16 year olds **Cannabis Use Assessment** Self-completion questionnaire **Psychotic-Like Experiences Assessment** PROD-Screen	**Prevalence of Cannabis Use** 5.6% **Prevalence of Psychotic-Like Experiences** NR	Early emotional and behavioural symptoms Gender Family type Parental social class based on occupation Regular tobacco use Use of other drugs Parental substance misuse disorder	Test of Analysis of Covariance Logistic Regression Analysis (Never vs. Ever)	Ever tried cannabis more likely to report 3 or more symptoms: Crude OR 2.79 (2.24 – 3.46) Proportion of those with high scores increased linearly by cannabis use category: OR for Linear Trend 1.42 (1.23 – 1.64) Logistic Regression (never vs ever): OR: 2.23 (1.70 – 2.94) High scores in prodromal symptoms increased linearly by cannabis use category	Test of Analysis of Covariance Ever tried cannabis had higher mean number of prodromal symptoms: 3.11 v. 1.88 t-test = 8.68 p<0.001 Test of analysis of covariance (never vs ever): F=38.73 p<0.001 Prodromal Symptoms by Cannabis Use Mean and SD Never: Mean = 1.88 SD = 1.94 Once: Mean = 2.97 SD = 2.53 2-4 Times: Mean = 3.08 SD = 2.61 5 Times or More: Mean = 3.68 SD = 2.90

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
						Regular Use: Mean = 3.11 SD = 2.15
5 **Continued Cannabis Use and Risk of Incidence and Persistence of Psychotic Symptoms: 10 Year Follow-up Cohort Study** Kuepper, R. et al. (2011) Germany Prospective Cohort	**Participants** 1,923 Age range: 14 to 24 year olds **Cannabis Use Assessment** Munich-Composite International Diagnostic Interview (DIA-X/M-CIDI) **Psychotic-Like Experiences Assessment** Munich-Composite International Diagnostic Interview (DIA-X/M-CIDI)	**Prevalence of Cannabis Use** Baseline: Lifetime use: 13% **Prevalence of Psychotic-Like Experiences** T2 lifetime: 23% T3 interval: 12%	Age Gender Socioeconomic status Use of other drugs Childhood trauma Urbanicity Pre-existing psychotic symptoms	Logistic Regression Models	Association Between Incident Cannabis Use at T2 (3.5 years after baseline) and Incident Psychotic Experiences at T3 (8.4 years after baseline) OR (95%) Unadjusted Whole Sample OR: 1.8 (1.3 – 2.4) $p < 0.001$ Adjusted Whole Sample (Age, sex, socioeconomic status, use of other drugs, childhood trauma and urban/rural environment) OR: 1.5 (1.1 – 2.1) $p = 0.018$ Unadjusted After Exclusion (Excludes individuals with baseline cannabis use and pre-existing psychotic symptoms) OR: 2.1 (1.3 – 3.4) $p = 0.004$ Adjusted After Exclusion (Age, sex, socioeconomic status, use of other drugs, childhood trauma and urban/rural environment) (Excludes individuals with baseline cannabis use and pre-existing psychotic symptoms)	NR

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					OR: 1.9 (1.1 – 3.1) p = 0.021 Association Between Continued Use of Cannabis (from baseline to T2) and Persistence of Psychotic Experiences at T2 and T3 OR (95%) Risk of Persistence of Psychotic Experiences and Cannabis Continuation Unadjusted At Baseline but not at T2 OR: 2.0 (0.95 – 4.4) p = 0.068 At T2 but not at Baseline OR: 1.9 (1.1 – 3.2) p = 0.022 At Baseline and T2 OR: 2.6 (1.5 – 4.6) p = 0.001 Risk of Persistence of Psychotic Experiences and Cannabis Continuation Adjusted (Age, sex, socioeconomic status, use of other drugs baseline and T2, childhood trauma, urban/rural environment) At Baseline but not at T2 OR: 2.1 (0.9 – 4.7) p = 0.078 At T2 but not at Baseline OR: 1.4 (0.8 – 2.5) p = 0.202 At Baseline and T2	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					OR: 2.2 (1.2 – 4.2) p = 0.016	
6 **Cannabis Use at a Young Age is Associated with Psychotic-Experiences** Schubart, C. et al. (2011) Netherlands Cross-sectional	**Participants** 17,698 Age range 18 to 25 year olds **Cannabis Use Assessment** Amount of Euros spent on cannabis **Psychotic-Like Experiences Assessment** Community Assessment of Psychic Experiences (CAPE)	**Prevalence of Cannabis Use** 67% **Prevalence of Psychotic-Like Experiences** NR	Age Gender Other drug use Level of education	Logistic Regression	**Amount of Euros/Week and 10% Total CAPE Score: OR (95%)** 0 to 3 Euros OR: 0.96 (0.82 – 1.13) 3 to 9 Euros OR: 1.46 (1.21 – 1.76) p < 0.05 9 to 25 Euros OR: 2.00 (1.68 – 2.38) p < 0.05 >25 Euros OR: 3.54 (2.94 – 4.26) p < 0.05 **Amount of Euros/Week and 10% Positive Dimension Score: OR (95%)** 0 to 3 Euros OR: 0.98 (0.84 – 1.15) 3 to 9 Euros OR: 1.72 (1.44 – 2.06) p < 0.05 9 to 25 Euros OR: 1.96 (1.65 – 2.33) p < 0.05	NR

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					>25 Euros OR: 3.54 (2.94 – 4.26) p < 0.05 **Initial Age OR for a Top 10% Total CAPE Score** >20 years OR: 1.18 (0.90 – 1.55) 18-20 years OR: 0.94 (0.78 – 1.13) 15-18 years 1.00 12-15 years OR: 1.16 (1.01 – 1.32) p < 0.05 <12 years OR: 1.82 (1.23 – 2.70) p < 0.05 **Initial Age OR for a Top 10% Positive Dimension Score** >20 years OR: 1.06 (0.76 – 1.48) 18-20 years OR: 0.84 (0.69 – 1.01) 15-18 years OR: 1.00 12-15 years OR: 1.15 (1.01 – 1.31) p < 0.05 <12 years OR: 3.05 (2.14 – 4.34) p < 0.05	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
7 **Linking Substance Use with Symptoms of a Subclinical Psychosis in a Community Cohort Over 30 Years** Roessler, W. et al. (2011) Switzerland Longitudinal	**Participants** 4,547 2,201 males 2,346 females **Cannabis Use Assessment** Structured Psychopathological Interview and Rating of the Social Consequences of Psychological Disturbances for Epidemiology (SPIKE) **Psychotic-Like Experiences Assessment** "Schizotypal Signs" "Schizophrenia Nuclear Symptoms"	**Prevalence of Cannabis Use** NR **Prevalence of Psychotic-Like Experiences** NR	Gender Familial background Socioeconomic status Family history of mental disorders Other family problems School problems Use of other drugs	Associations between substance use and psychotic symptoms were evaluated with discrete-time hazard models, i.e. survival analyses Discrete-time hazard models for bivariate associations which rely on binary **logistic regressions** with longitudinal data. Initially conducted a series of bivariate analysis of substance use and psychotic symptoms for separate substance-use variables, each was adjusted. In the multivariate analysis (models) included all such variables that shown a significant association in bivariate analysis.	**Discrete-Time Hazard Models for Bivariate Associations between Substance Use and "Schizotypal Signs"** Frequency of Cannabis Use in Adolescence OR (95%) Casual Use OR: 1.80 (1.22 – 2.66) p = 0.003 Frequency of Cannabis Use in Adolescence OR (95%) Regular Use OR: 2.29 (1.32 – 3.97) p = 0.003 Frequency of Cannabis Use in Adulthood OR (95%) Casual Use OR: 1.47 (0.94 – 2.29) Frequency of Cannabis Use in Adulthood OR (95%) Regular Use OR: 1.80 (1.00 – 3.22) **Discrete-Time Hazard Models for Bivariate Associations between Substance Use and "Schizophrenia Nuclear Symptoms"** Frequency of Cannabis Use in Adolescence OR (95%) Casual Use OR: 1.13 (0.74 – 1.73) Frequency of Cannabis Use in Adolescence OR (95%) Regular Use OR: 1.73 (0.96 – 3.11)	NR

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					Frequency of Cannabis Use in Adulthood OR (95%) Casual Use OR: 1.59 (1.03 – 2.46) Frequency of Cannabis Use in Adulthood OR (95%) Regular Use OR: 1.77 (0.96 – 3.24) **Discrete-Time Hazard Models for Multivariate Associations between Substance Use and "Schizotypal Signs"** Frequency of Cannabis Use in Adolescence OR (95%) Casual Use OR: 1.80 (1.24 – 2.59) p = 0.002 Frequency of Cannabis Use in Adolescence OR (95%) Regular Use OR: 2.60 (1.59 – 4.23) p <0.001	
8 **Adolescent Bullying, Cannabis Use and Emerging Psychotic-Experiences: A Longitudinal General Population Study** Mackie, C. et al. (2013) UK Prospective Longitudinal	**Participants** 1,098 **Cannabis Use Assessment** Reckless Behaviour Questionnaire **Psychotic-Like Experiences Assessment** Diagnostic Interview Schedule	**Prevalence of Cannabis Use** Low: 22.7% Elevated: 38.6% Increasing: 38% **Prevalence of Psychotic-Like Experiences** Low: 86.9% Elevated: 4.7% Increasing: 8.4%	Illicit Drug Use Depression Cigarette Alcohol use Previous psychotic experiences Socioeconomic level Gender Ethnicity	Multinomial Logistic Regressions	Class Trajectory Model: Psychotic-Like Experiences (Low, Elevated and Increasing) **Associations Between Cannabis Use at Time 1 and Trajectory Class** **Elevated vs. Low RR (95% CI)** Cannabis Use Onset Ages 14 and 16 RR: 1.66 (0.67-4.15) Cannabis Use Onset Prior to 14 RR: 2.54 (1.22-5.23) p<0.05	**CU onset 14-16** Low: 0.17 Elevated: 0.16 Increasing: 0.23 **CU before 14** Low: 0.11 Elevated: 0.19 Increasing: 0.43 **CU Frequency Once** Low: 0.10 Elevated: 0.01 Increasing: 0.04

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
			Bullying		Cannabis Use Frequency Once RR: 2.02 (0.92-4.41) Cannabis Use Frequency >2 Times RR: 2.30 (1.01-5.24) p<0.05 **Increasing vs. Low RR (95% CI)** Cannabis Use Onset Ages 14 and 16 RR: 1.99 (1.04-3.82) p<0.05 Cannabis Use Onset Prior to 14 RR: 2.16 (1.20-3.90) p<0.05 Cannabis Use Frequency Once RR: 1.90 (1.00-3.73) p<0.05 Cannabis Use Frequency >2 Times RR: 2.22 (1.25-3.96) p<0.01 **Effect of Cannabis Use on Subsequent Changes in Psychotic Experiences in Each Trajectory Class** **Trajectory Class: Low** Cannabis Use Onset Ages 14 and 16 RR: 0.17 (0.06 – 0.28) p < 0.01 Cannabis Use Onset Prior to 14 RR: 0.11 (0.01 – 0.22)	**CU Frequency >2 Times** Low: 0.24 Elevated: 0.21 Increasing: 0.04

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					p < 0.05 Cannabis Use Frequency Once RR: 0.10 (0.01 – 0.20) p < 0.05 Cannabis Use Frequency >2 Times RR: 0.24 (0.13 – 0.35) p < 0.01 **Trajectory Class: Elevated** Cannabis Use Onset Ages 14 and 16 RR: 0.16 (-0.79 – 1.11) Cannabis Use Onset Prior to 14 RR: 0.19 (-0.63 – 1.00) Cannabis Use Frequency Once RR: 0.01 (-0.80 – 0.82) Cannabis Use Frequency >2 Times RR: 0.21 (-0.69 – 1.10) **Trajectory Class: Increasing** Cannabis Use Onset Ages 14 and 16 RR: 0.23 (-0.25 – 0.72) Cannabis Use Onset Prior to 14 RR: 0.43 (0.01 – 0.87) p < 0.05 Cannabis Use Frequency Once RR: 0.04 (-0.50 – 0.58) Cannabis Use Frequency >2 Times RR: 0.50 (0.07 – 0.92)	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
9 **Associations of Cannabis and Cigarette Use with Psychotic-Experiences at Age 18: Findings from the AVON Longitudinal Study of Parents and Children** Gage, S. et al. (2014) UK Cohort Study	**Participants** 1,756 **Cannabis Use Assessment** Self-report questionnaire **Psychotic-Like Experiences Assessment** Semi-structured interview (PLIKSi: Zammit et al. 2013)	**Prevalence of Cannabis Use** 27.4% **Prevalence of Psychotic-Like Experiences** 5.5%	Pre-birth confounders Childhood confounders Alcohol use Cigarette use Other drug use	Logistic Regression	Ordinal Logistic Regression of Cumulative Cannabis Use at age 16 and Psychotic Experiences at age 18 (95%) Excluding Psychotic Experiences at 12: Model 1: Psychotic Experiences at 18 by categorical cumulative cannabis use at 18 OR: 1.48 (1.018 – 1.86) p = 0.001 Model 2: As model 1 with additional adjustment for pre-birth confounders OR: 1.53 (1.21 – 1.92) p < 0.001 Model 3: As model 2 with additional adjustment for childhood confounders OR: 1.57 (1.23 – 2.00) p < 0.001 Model 4a: As model 3 with additional adjustment for cigarette use OR: 1.27 (0.91 – 1.76) p = 0.160 Model 4b: As model 3 with additional adjustments for alcohol use OR: 1.57 (1.19 – 2.08) p = 0.002 Model 4c: As model 3 with additional adjustment for illicit drug use (other than cannabis) OR: 1.25 (0.91 – 1.73)	NR

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					p = 0.165 Model 5: As model 3 with additional adjustment for cigarette, alcohol and other illicit drug use OR: 1.12 (0.76 – 1.65) p = 0.553 Excluding Psychotic Experiences at 12 and 16: Model 1: Psychotic Experiences at 18 by categorical cumulative cannabis use at 18 OR: 1.35 (0.98 – 1.86) p = 0.070 Model 2: As model 1 with additional adjustment for pre-birth confounders OR: 1.40 (1.01 – 1.95) p = 0.043 Model 3: As model 2 with additional adjustment for childhood confounders OR: 1.50 (1.07 – 2.10) p = 0.019 Model 4a: As model 3 with additional adjustment for cigarette use OR: 1.08 (0.69 – 1.69) p = 0.744 Model 4b: As model 3 with additional adjustments for alcohol use OR: 1.62 (1.10 – 2.39) p = 0.015	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					Model 4c: As model 3 with additional adjustment for illicit drug use (other than cannabis) OR: 1.30 (0.84 – 2.01) p = 0.247 Model 5: As model 3 with additional adjustment for cigarette, alcohol and other illicit drug use OR: 1.09 (0.65 – 1.82) p = 0.751	
10 **Concurrent and Sustained Cumulative Effects of Adolescent Marijuana Use on Subclinical Psychotic Symptoms** Bechtold, J. et al. (2016) USA Longitudinal Study	**Participants** 1,009 **Cannabis Use Assessment** Youth-reported substance use questionnaire **Psychotic-Like Experiences Assessment** Youth Self Report: Subclinical psychotic symptoms (Symptoms Not Disorder)	**Prevalence of Cannabis Use** NR **Prevalence of Psychotic-Like Experiences** NR	Use of other drugs Internalizing problems Externalizing problems	Fixed-effects regressions used to examine the within-individual association between changes in weekly marijuana use and psychotic symptoms between ages 13 and 18. Poisson fixed-effects regression model for total subclinical symptoms and logistic fixed-effects regression models (for binary symptom subtypes) were used. **<u>Logistic</u>** Incidence rate ratios are reported for total symptoms and odds ratio are reported for symptom subtypes. **<u>Linear</u>** Three models were run.	**Total Subclinical Psychotic Symptoms** Current weekly use without covariates: 1.37 (1.16 – 1.62) p<0.001 Years of prior weekly use without covariates: 1 Year: 1.20 (0.97 – 1.48) _>2 Years: 1.45 (1.09 – 1.93) p<0.05 Test of linear trend without covariates: 1.20 (1.05 – 1.38) p<0.01 Current weekly use with covariates: 1.12 (0.93 – 1.35) Years of prior weekly use with covariates:	NR

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
				To examine the possibility of reverse causation, logistic fixed-effects regressions examined whether changes in current and prior subclinical psychotic symptoms predicted changes in weekly marijuana use. Linear Regression and Logistic Regression Multiple Linear Regression Linear trend analysis the number of years of prior use was treated as a continuous predictor	1 Year: 1.15 (0.91 – 1.46) _>2 Years: 1.51 (1.08 – 2.11) P<0.05 Test of linear trend with covariates: 1.21 (1.03 – 1.42) p<0.05 **Effect of Years of Prior Weekly Marijuana Use** No Marihuana Use in the Past Year Incidence Rate Ratio or Odds Ratio Total subclinical psychotic symptoms 1.29 (1.00 – 1.66) P<0.05 Paranoia 2.12 (1.16 – 3.89) P<0.05 Hallucinations 2.58 (1.07 – 5.20) P<0.05 Bizarre Thinking 1.16 (0.64 – 2.09) Some Marihuana Use in Past Year Incidence Rate Ratio or Odds Ratio	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					Total subclinical psychotic symptoms 1.19 (1.00 – 1.41) P<0.05 Paranoia 2.41 (1.55 – 3.74) P<0.001 Hallucinations 1.73 (0.93 – 3.22) P<0.09 Bizarre Thinking 1.08 (0.71 – 1.64) **Lifetime Psychotic Disorder** Years of weekly marijuana use: Odds Ratio 95% CI 1 – 2 Years: 0.85 (0.26 – 2.78) _>3 Years: 3.63 (1.22 – 10.83) P<0.05 Test of linear trend: 1.61 (0.89 – 2.93)	
11 **Cannabis Use and Psychotic-Like Experiences Trajectories During Early Adolescence** Bourque, J. et al. (2017)	**Participants** 3,069 13 year olds **Cannabis Use Assessment** Detection of Alcohol and Drug Problems in Adolescence **Psychotic-Like Experiences Assessment**	**Prevalence of Cannabis Use** NR **Prevalence of Psychotic-Like Experiences** NR	Age Gender Socioeconomic Status Sleep problems Anxiety	Multinomial and Binary Logistic Regressions Linear Regression to estimate the relationship between growth in cannabis use, growth in potential mediators and psychotic-like	Multinomial Logistic Regression Models of Cannabis Use Growth Over 13 – 16 Years Old Predicting Youth's Membership in the PLE Trajectory Class Odds Ratio (95% CI) Model 1 Cannabis Intercept High Decreasing Vs. Low Decreasing	NR

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
Prospective Longitudinal	Adolescent Psychotic Symptom Screener (Psychotic-Like Experiences Not Disorder)			experiences trajectory membership	OR: 1.01 (0.33 – 3.03) Moderate Increasing Vs. Low Decreasing OR: 0.38 (0.09 – 1.66) Moderate Increasing Vs. High Decreasing OR: 0.37 (0.06 – 2.29) Model 1 Cannabis Slope High Decreasing Vs. Low Decreasing OR: 1.00 (0.53 – 1.87) Moderate Increasing Vs. Low Decreasing OR: 3.26 (1.50 – 7.07) p < .01 Moderate Increasing Vs. High Decreasing OR: 3.28 (1.47 – 7.27) p < .01 Model 2: Adjusted for Cumulative Cigarette Use Cannabis Intercept High Decreasing Vs. Low Decreasing OR: 0.95 (0.28 – 3.17) Moderate Increasing Vs. Low Decreasing OR: 0.28 (0.05 – 1.54) Moderate Increasing Vs. High Decreasing OR: 0.29 (0.04 – 2.40) Model 2 Cannabis Slope	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					High Decreasing Vs. Low Decreasing OR: 0.92 (0.48 – 1.73) Moderate Increasing Vs. Low Decreasing OR: 2.59 (1.11 – 6.03) p < .05 Moderate Increasing Vs. High Decreasing OR: 2.82 (1.23 – 6.48) p < .05	
12 **Cannabis Use, Poly-substance Use and Psychosis Spectrum Symptoms in a Community-Based Sample of US Youth** Jones, J., et al. (2017) USA Cross-sectional	Participants 4,208 Age range: 14-21 years old Cannabis Use Assessment: Abbreviated and locally computerized version of the Minnesota Centre for Twin and Family Research self-report substance use measure Psychotic-Like Experiences: GOASSSESS, a computerized, structured interview adapted from the Kiddie Schedule for Affective Disorders and Schizophrenia	Prevalence of Cannabis Use 28% Prevalence of Psychotic-Like Experiences 19%	Age Gender Racial minority status Maternal education Reading subtest score Significant symptoms of mood, anxiety and behavioural disorders Trauma exposure Intellectual function Family history of substance abuse	Logistic Regression	Occasional Cannabis Use: Unadjusted 1.23 (1.02-1.49) Additional adjustment for alcohol frequency group, tobacco frequency group and past year other substance use 1.01 (.75-1.34) Frequent Cannabis Use: Unadjusted 2.78 (2.09-3.72) Additional adjustment for alcohol frequency group, tobacco frequency group and past year other substance use 1.51 (.97-2.36) Early Cannabis Use: Unadjusted 2.07 (1.62-2.64) Additional adjustment for early alcohol use, early tobacco use,	NA

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
					past year cannabis use and lifetime use of other substance 1.28 (.78-2.11) Later Cannabis Use: Unadjusted 1.19 (.92-1.54) Additional adjustment for early alcohol use, early tobacco use, past year cannabis use and lifetime use of other substance 1.14 (.73-1.79)	
13 **Cannabis Use and Psychosis: The Impact of Polydrug Use** Shevlin, M. et al. (2017) Denmark Retrospective Birth Cohort	Participants 2,980 Age range: 24 years old Cannabis Use Assessment: "Have you ever tried…" Psychotic Disorder Assessment: ICD-10	Prevalence of Cannabis Use 31.6% Cannabis Only 20% Cannabis and Other Drugs Prevalence of Psychotic-Like Experiences 0.5%	Gender Parental Psychosis Use of other drugs	Chi-square Binary Logistic Regression	Cannabis Only 0.69 (0.12-4.07) Cannabis and Other Drug 5.96 (1.71-20.75)	Cannabis Only -0.37 Cannabis and Other Drug 1.79
14 **Associations of Combined Patterns of Tobacco and Cannabis Use in Adolescence with Psychotic Experiences** Jones, H., et al. (2018) England	Participants 5,300 Age range: birth cohort, measures of cannabis use were collected at 6 time points between ages 14-19 Cannabis Use Assessment: No use of cannabis or cigarettes Cigarette only Cannabis with or without Psychotic-Like Experiences Assessment:	NR	Gender Family history of schizophrenia or depression Family history of drug use Maternal or parental smoking during pregnancy Maternal education Highest parental social class IQ (8 years old)	Longitudinal Latent Class Analysis: to identify number of latent classes that adequately explain the relationship between the observed variables Multinomial Regression Logistic Regression	Early Onset of Cannabis (with or without cigarettes): Unadjusted 3.79 (1.73-8.31) Adjusted for sex, maternal education, emotional and behavioural problems and maternal cigarette smoking during pregnancy 3.70 (1.66-8.25)	NA

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
Longitudinal Cohort Study	Semi-structured psychosis-like symptom interview (PLIKSi)		Childhood trauma or experiencing bullying Emotional and behavioural problems Alcohol use		Late Onset of Cannabis Use (with or without cigarettes): Unadjusted 3.05 (1.69-5.53) Adjusted for sex, maternal education, emotional and behavioural problems and maternal cigarette smoking during pregnancy 2.97 (1.63-5.40)	
15 **Adolescent Cannabis Use, Baseline Prodromal Symptoms and the Risk of Psychosis** Mustonen, A., et al. (2018) Finland Birth Cohort Longitudinal	Participants 6,534 Age range: data of cannabis use collected when participants were aged 15-16 years old. Cannabis Use Assessment: Lifetime use and frequency of use (never, once, 2-4 times, 5 times or more or regularly Psychosis Diagnosis Assessment: ICD-10 Prodromal Symptoms Assessment: PROD-Screen	Prevalence of Cannabis Use 5.7% Prevalence of Prodromal Symptoms 30.5%	Tobacco Use Substance Use Family Structure Place of Residence Family Socioeconomic Status Parental Psychosis	Cox-Regression Analysis (hazard ratios with 95%CI) Logistic Regression Analysis	Ever Cannabis Use 2.85 (1.73-4.67) Frequency of Cannabis Use 2-4 times 3.03 (1.33-6.90) 5 times+ 6.47 (3.01-13.91) Model 1: PROD-Screen and Frequency of Cannabis Use 5 times+ 4.38 (2.00-9.59) Model 2: PROD-Screen and Other Substance Use, Frequent Alcohol Use and Daily Tobacco Use 5 times+ 3.16 (1.21-8.29) Model 3: Model 2 + Parental Psychosis 5 times+ 3.02 (1.14-7.98)	NA

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Odds Ratio	Unstandardized Beta
16 **Acute Mental Health Symptoms in Adolescent Marijuana Users** Levy, S. et al. (2019) USA Cross-sectional	Participants 527 Age range: 14-18 years old Cannabis Use Assessment: Standardized questions about symptoms of cannabis use disorder based on the modified World Mental Health Composite International Diagnostic Interview Psychotic-Like Experiences Assessment: Two questions: "In the past 12 months, how often have you felt anxious or paranoid during or after using marijuana?" "In the past 12 months, how often have you seen, felt, or heard things that were not really there (i.e., hallucinations) during or after using marijuana?"	Prevalence of Cannabis Use 47.9% monthly or more Prevalence of Psychotic-Like Experiences 42.9%	Age Gender Race / Ethnicity Socioeconomic Status General health status	Chi-Square Logistic Regression Models adjusted for: Age Sex Race / Ethnicity	Cannabis Use Disorder vs. Non-Diagnosis and Hallucinations: 3.76 (1.69-8.34) Cannabis Use Disorder vs. Non-Diagnosis and Paranoia or Anxiety: 3.15 (1.46-6.78) Past Year Frequency of Cannabis Use (Monthly+) and Hallucinations: 3.81 (1.71-8.50) Past Year Frequency of Cannabis Use (Monthly+) and Paranoia or Anxiety: 3.30 (1.58-6.89)	NA

9.3.2. Table 2. Studies Included in Systematic Review: Linear Regression Analysis

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
1 **Cannabis Use in Adolescence and Risk for Adult Psychosis: Longitudinal Prospective Study** Arseneault, L. et al. (2002) New Zealand Prospective Longitudinal Cohort	**Participants** 759 Age range: 11-26 years old **Cannabis Use Assessment** Controls: Never or once Cannabis users at age 15: three times or more Cannabis users at age 18: three times or more **Psychotic-Like Experiences Assessment** Standardized interview scheduled (DSM-IV) (Symptoms and Disorder)	**Prevalence of Cannabis Use** NR **Prevalence of Psychotic-Like Experiences** NR	Socioeconomic status Gender Use of other drugs PLE's at 11	Multiple Linear Regression Logistic Regression	NR	**Association between Cannabis Use in Adolescence and Schizophrenia Symptoms** (Scores 0-58) Model 1: Cannabis Use Only Cannabis Users by 15: b = 6.91 SE = 0.91 p = 0.001 Cannabis Users by 18: b = 1.04 SE = 0.40 p = 0.009 Model 2: Adds to Model 1 Controls for Childhood Psychotic Symptoms Weak Psychotic Symptoms at age 11: b = 0.68 SE = 0.53 p = 0.201 Strong Psychotic Symptoms at age 11: b = 5.16 SE = 1.39 p = 0.001 Cannabis Users by 15: b = 6.56 SE = 0.91 p = 0.001 Cannabis Users by 18:

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
						b = 1.03 SE = 0.39 p = 0.009 Model 3: Adds to Model 1 Controls for Other Drug Use Other drug users at 15 to 18: b = -0.3 SE = 0.69 p = 0.615 Cannabis Users by 15: b = 7.2 SE = 1.07 p = 0.001 Cannabis Users by 18: b = 1.1 SE = 0.42 p = 0.008
2 **Cannabis Dependence and Psychotic Symptoms in Young People** Fergusson, D.M. et al. (2003) New Zealand Longitudinal	**Participants** 1,053 **Cannabis Use Assessment** Composite International Diagnostic Interview (CIDI) Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) **Psychotic-Like Experiences Assessment** Items from the Symptom Checklist 90 (SCL-90) (Symptoms not Disorder)	**Prevalence of Cannabis Use** Dependence: 10% **Prevalence of Psychotic-Like Experiences**	Sociodemographic background Family functioning Parental adjustment Individual characteristics Prior psychotic symptoms and mental health Use of other drugs Major depression Anxiety disorders Affiliation with deviant peers Adverse life events Age of leaving the family home	**Logistic Regression** Negative binomial regression model to predict the logarithm of the psychotic symptom count from cannabis dependence at each age. Linkages between measures of cannabis dependence and psychotic symptom scores were modelled using a generalized estimating equation (GEE) approach. Incidence Rate Ratio interpreted as the relative increase in the rate of psychotic symptoms for those who were cannabis	Mean Psychotic Symptoms (Past Month) by Cannabis Dependence (Past 12 Months) at Age 18 and 21 At 18 Cannabis Dependence: *No:* Mean: 0.78 *Yes:* Mean: 2.89 p < 0.0001 Rate Ratio (95%) 3.7 (2.5 – 5.0) At 21 Cannabis Dependence: *No:* Mean: 0.87 *Yes:* Mean: 2.02 p < 0.0001 Rate Ratio (95%) 2.3 (1.7 – 3.2)	Estimated Association Between Cannabis Dependence and Psychotic Symptoms after Adjustment for Confounding Factors **Regression Parameter** B = 0.570 SE = 0.189 p < 0.005 Rate Ratio (95%) 1.8 (1.2 – 2.6)

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
				dependent in comparison to those who were not.		
3 **Early Adolescent Cannabis Exposure and Positive and Negative Dimensions of Psychosis** Stefanis, N. et al. (2004) Greece Cross-Sectional	**Participants** 3,500 19 year olds **Cannabis Use Assessment** Cannabis lifetime frequency use (never, once, 2-4 times, 5 times or more) Systematic Use: Daily or Almost Daily **Psychotic-Like Experiences Assessment** Community Assessment of Psychic Experiences (CAPE)	**Prevalence of Cannabis Use** Lifetime frequency: 6% Once: 2.0% 2 to 4 times: 1.4% 5 times or more: 1.5% Systematic use: 0.9% **Prevalence of Psychotic-Like Experiences** Mean SD Scores: Paranoia: 0.20 (0.24) Grandiosity: 0.20 (0.40) First Rank Symptoms: 0.10 (0.17) Hallucinations: 0.02 (0.15)	Other dimensions CAPE Gender School grade obtained Use of other drugs	**Linear Model** Associations were expressed as regression coefficients of cannabis use in multiple regression models of continuous scores of positive, negative and depression dimensions. To examine whether effects of cannabis increased linearly with and without squared cannabis life-time frequency of use were compared by likelihood radio test.	NR	Association Lifetime Frequency of Cannabis Use and Psychosis Hallucinations and =5 times use: B = 0.27 p = 0.058 Hallucinations and Systematic use: B = 1.39 p = 0.000 Paranoia and =5 times: B = 0.64 p = 0.000 Paranoia Systematic use: B = 0.96 p = 0.000 Paranoia Regression Coefficient Linear Trend Unadjusted: B = 0.23 p = 0.000 Paranoia Regression Coefficient Linear Trend Adjusted: B = 0.09 p = 0.003 Grandiosity and =5 times use: B = 0.36 p = 0.010 Grandiosity and Systematic use: B = 0.37 p = 0.037

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
						First Rank and =5 times use: B = 0.50 p = 0.000 First Rank and Systematic use: B = 0.55 p = 0.002 First Rank Regression Coefficient Linear Trend Unadjusted: B = 0.17 p = 0.000 First Rank Regression Coefficient Linear Trend Adjusted: B = 0.06 p = 0.000 Effect of Cannabis Age First Use on Psychosis Dimension Not Adjusted for Frequency Use Hallucinations <_15: B = 1.16 p = 0.000 _>16: B = 0.15 p = 0.076 Paranoia <_15: B = 0.91 p = 0.000 >_16: B = 0.36 p = 0.000

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
						Grandiosity <_15: B = 0.86 p = 0.000 >_16: B = 0.27 p = 0.001 First Rank <_15: B = 0.84 p = 0.000 >_16: B = 0.33 p = 0.000 Adjusted for Frequency Use Hallucinations <_15: B = 0.74 p = 0.001 _>16: B = -0.18 p = 0.25 Paranoia <_15: B = 0.56 p = 0.10 >_16: B = 0.09 p = 0.56 Grandiosity <_15: B = 0.74 p = 0.001 >_16:

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
						B = 0.18 p = 0.18 First Rank <_15: B = 1.09 p = 0.000 >_16: B = 0.52 p = 0.001
4 **The Associations between Early Cannabis Use and Psychotic-Like Experiences in a Community Adolescent Sample** Hides, L. et al. (2009) Australia Cross-Sectional Look for P Lifetime Use	**Participants** 880 Age range: 13 to 19 year olds **Cannabis Use Assessment** Youth Risk Behaviour Survey (YRBS) **Psychotic-Like Experiences Assessment** Community Assessment of Psychiatric Experiences (CAPE)	**Prevalence of Cannabis Use** 10% **Prevalence of Psychotic-Like Experiences** NR	Gender Depression Alcohol use Tobacco Use of other drugs	General Linear Models	Means and SD of Psychotic-Like Experiences and Cannabis Exposure Positive Scale Total Frequency of Cannabis Use Last Year No Use Mean = 31.2 SD = 6.9 p<0.05 Lifetime Use Mean = 33.8 SD = 8.3 Rarely Use: Mean = 35.8 SD = 8.7 p<0.05 Frequent Use: Mean = 29.4 SD = 5.7 p<0.05	**NR**

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
5 **Early Exposure to Cannabis and Risk for Psychosis in Young Adolescents in Trinidad** Konings, M. et al. (2008) Trinidad y Tobago Cross-Sectional check info with paper	**Participants** 472 Age range: 12 to 23 year olds **Cannabis Use Assessment** Questionnaire on past and current cannabis use **Psychotic-Like Experiences Assessment** Community Assessment of Psychic Experiences	**Prevalence of Cannabis Use** 21% **Prevalence of Psychotic-Like Experiences** NR	Age School type Ethnicity Gender Use of other drugs	Multiple Linear Regression	**NR**	Cannabis use before 14 years old was significantly associated with higher levels of psychotic symptoms: <14 Not Adjusted: b = 0.39 CI = 0.04 – 0.74 P = 0.029 Adjusted: b = 0.71 CI = 0.22 – 1.19 p = 0.004 >14 b = -0.11 CI = -0.57, 0.36 p = 0.66
6 **Early Cannabis Use and Schizotypal Personality Disorder Symptoms from Adolescence to Middle Adulthood** Anglin, D. et al. (2012) USA Longitudinal (Symptoms not Disorder)	**Participants** 804 410 men Age range: 9-18 years old **Cannabis Use Assessment** Users: At least monthly use Non-users: Experimented once or twice Early CU: before 14 years old **Psychotic-Like Experiences Assessment** Children in the Community Self Report Schizotypal Personality Disorder Scale	**Prevalence of Cannabis Use** 70% **Prevalence of Psychotic-Like Experiences** NR	Other type of psychopathology Use of other drugs Cigarette use Gender Socioeconomic status	Hierarchical Linear Regression	d = 0.53 p<0.001	Model 1: Effects of Early Cannabis Use on Average over the Schizotypal Symptoms Trajectory Independent of Age, Gender and Socioeconomic status effects. Mean Schizotypal Symptoms at Trajectory Mean Age 23 b = -2.8 SE = .04 Early Cannabis Use b = .24 p<.01 SE = .08 Model 2: Schizotypal Symptoms Added at Mean Age 13.7 to Predictors

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
						Mean Schizotypal Symptoms at Trajectory Mean Age 23 b = -.25 SE = .04 Early Cannabis Use b =.20 p<.05 SE = .08 Model 3: Effects of Early Cannabis Use in Presence of Other Adolescent Psychopathology Mean Schizotypal Symptoms at Trajectory Mean Age 23 b = -.36 SE = .04 Early Cannabis Use b = .23 p<.01 SE = .08 Model 4: Cigarettes and Other Drug Use Taken into Account Mean Schizotypal Symptoms at Trajectory Mean Age 23 b = -.27 SE = .05 Early Cannabis Use b = .18 p<.05 SE = .09 All Models: p<.0001

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
7 **Cannabis Use and Subclinical Positive Psychotic Experiences in Early Adolescence: Findings from a Dutch Survey** Van Gastel, W. et al. (2011) Netherlands Observational Cross-sectional	**Participants** 4,552 Age range: 12 to 16 year olds **Cannabis Use Assessment** Frequency of cannabis use (never, ever but not past year, once or twice during past year, between 3 and 39 times) **Psychotic-Like Experiences Assessment** Community Assessment of Psychic Experiences (CAPE)	**Prevalence of Cannabis Use** 14% **Prevalence of Psychotic-Like Experiences** NR	Age Gender Household composition Family affluence Social support from father, mother and friends Alcohol use Ethnicity Urbanization	Multivariate Linear Regression	Stand. Regression Est. Unadjusted Model: B = 0.138 p = 0.000 Adjusted Model: B = 0.088 p = 0.000 CU and Age: B = 0.081 p = 0.000 Cannabis use and subclinical positive psychotic experiences are strongest for youngest children. Level of Cannabis Use and CAPE: Discontinued use: B = 0.061 p = 0.000 Experimental Use: B = 0.037 p = 0.018 Regular Use: B = 0.048 p = 0.005 Heavy Use: B = 0.065 p = 0.000 Age and Cannabis Use on CAPE: Discontinued use: B = -0.080	NR

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
					p = 0.038 Experimental use: B = -0.0337 p = 0.000 Regular Use: B = -0.586 p = 0.000 Heavy Use: B = -0.376 p = 0.001	
8 **Cannabis Use and Vulnerability for Psychosis in Early Adolescence-a TRIALS Study** Griffith-Lendering, M. et al. (2012) Netherlands Longitudinal	**Participants** 2,230 Female: 1,133 Male: 1,097 **Cannabis Use Assessment** Self-report items regarding frequency in the last year **Psychotic-Like Experiences Assessment** Youth Self-report subscales	**Prevalence of Cannabis Use** T2: 5.8% T3: 25.7% T4: 34.6% **Prevalence of Psychotic-Like Experiences** NR	Parental psychopathology Use of other drugs: Tobacco and alcohol SES	Path analysis to address the temporal order of cannabis use and psychosis vulnerability after including covariates (gender, familial vulnerability for externalizing disorders, alcohol and tobacco use).	Cannabis Use at T3 predicted Psychosis Vulnerability at T4 z = 2.6 p<0.05	**NR**
9 **Concurrent and Sustained Cumulative Effects of Adolescent Marijuana Use on Subclinical Psychotic Symptoms** Bechtold, J. et al. (2016)	**Participants** 1,009 **Cannabis Use Assessment** Youth-reported substance use questionnaire **Psychotic-Like Experiences Assessment** Youth Self Report: Subclinical psychotic symptoms (Symptoms Not Disorder)	**Prevalence of Cannabis Use** NR **Prevalence of Psychotic-Like Experiences** NR	Use of other drugs Internalizing problems Externalizing problems	Fixed-effects regressions used to examine the within-individual association between changes in weekly marijuana use and psychotic symptoms between ages 13 and 18. Poisson fixed-effects regression model for total subclinical symptoms and logistic fixed-effects	**Total Subclinical Psychotic Symptoms** Current weekly use without covariates: 1.37 (1.16 – 1.62) p<0.001 Years of prior weekly use without covariates: 1 Year: 1.20 (0.97 – 1.48)	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
USA Longitudinal Study				regression models (for binary symptom subtypes) were used. **<u>Logistic</u>** Incidence rate ratios are reported for total symptoms and odds ratio are reported for symptom subtypes. **<u>Linear</u>** Three models were run. To examine the possibility of reverse causation, logistic fixed-effects regressions examined whether changes in current and prior subclinical psychotic symptoms predicted changes in weekly marijuana use. Linear Regression and Logistic Regression Multiple Linear Regression Linear trend analysis the number of years of prior use was treated as a continuous predictor	_>2 Years: 1.45 (1.09 – 1.93) p<0.05 Test of linear trend without covariates: 1.20 (1.05 – 1.38) p<0.01 Current weekly use with covariates: 1.12 (0.93 – 1.35) Years of prior weekly use with covariates: 1 Year: 1.15 (0.91 – 1.46) _>2 Years: 1.51 (1.08 – 2.11) P<0.05 Test of linear trend with covariates: 1.21 (1.03 – 1.42) p<0.05 **Effect of Years of Prior Weekly Marijuana Use** No Marihuana Use in the Past Year Incidence Rate Ratio or Odds Ratio Total subclinical psychotic symptoms 1.29 (1.00 – 1.66) P<0.05 Paranoia 2.12 (1.16 – 3.89)	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
					P<0.05 Hallucinations 2.58 (1.07 – 5.20) P<0.05 Bizarre Thinking 1.16 (0.64 – 2.09) Some Marihuana Use in Past Year Incidence Rate Ratio or Odds Ratio Total subclinical psychotic symptoms 1.19 (1.00 – 1.41) P<0.05 Paranoia 2.41 (1.55 – 3.74) P<0.001 Hallucinations 1.73 (0.93 – 3.22) P<0.09 Bizarre Thinking 1.08 (0.71 – 1.64) **Lifetime Psychotic Disorder** Years of weekly marijuana use: Odds Ratio 95% CI 1 – 2 Years: 0.85 (0.26 – 2.78) _>3 Years: 3.63 (1.22 – 10.83) P<0.05 Test of linear trend:	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
					1.61 (0.89 – 2.93)	
10 **Cannabis Use and Psychotic-Like Experiences Trajectories During Early Adolescence** Bourque, J. et al. (2016) Prospective Longitudinal (Poster double check info from paper)	**Participants** 3,069 13 year olds **Cannabis Use Assessment** Detection of Alcohol and Drug Problems in Adolescence **Psychotic-Like Experiences Assessment** Adolescent Psychotic Symptom Screener (Psychotic-Like Experiences Not Disorder)	**Prevalence of Cannabis Use** NR **Prevalence of Psychotic-Like Experiences** NR	Age Gender Socioeconomic Status Sleep problems Anxiety	Multinomial and Binary Logistic Regressions Linear Regression to estimate the relationship between growth in cannabis use, growth in potential mediators and psychotic-like experiences trajectory membership	Multinomial Logistic Regression Models of Cannabis Use Growth Over 13 – 16 Years Old Predicting Youth's Membership in the PLE Trajectory Class Odds Ratio (95% CI) Model 1 Cannabis Intercept High Decreasing Vs. Low Decreasing OR: 1.01 (0.33 – 3.03) Moderate Increasing Vs. Low Decreasing OR: 0.38 (0.09 – 1.66) Moderate Increasing Vs. High Decreasing OR: 0.37 (0.06 – 2.29) Model 1 Cannabis Slope High Decreasing Vs. Low Decreasing OR: 1.00 (0.53 – 1.87) Moderate Increasing Vs. Low Decreasing OR: 3.26 (1.50 – 7.07) $p < .01$	

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
					Moderate Increasing Vs. High Decreasing OR: 3.28 (1.47 – 7.27) p < .01 Model 2: Adjusted for Cumulative Cigarette Use Cannabis Intercept High Decreasing Vs. Low Decreasing OR: 0.95 (0.28 – 3.17) Moderate Increasing Vs. Low Decreasing OR: 0.28 (0.05 – 1.54) Moderate Increasing Vs. High Decreasing OR: 0.29 (0.04 – 2.40) Model 2 Cannabis Slope High Decreasing Vs. Low Decreasing OR: 0.92 (0.48 – 1.73) Moderate Increasing Vs. Low Decreasing OR: 2.59 (1.11 – 6.03) p < .05 Moderate Increasing Vs. High Decreasing OR: 2.82 (1.23 – 6.48) p < .05	
11 **Age Moderates the Association between Frequent Cannabis Use and Negative Schizotypy Over Time**	**Participants** 155 Age range: 14-24 years old **Cannabis Use Assessment** Lifetime use Past 6 months use		Tobacco Use Alcohol Use Use of other drugs Current Psychological Distress	Generalized Estimating Equation Regressions	**NR**	**Interaction Between Time, Age and Frequent Cannabis Use** Wald X^2=9.5, p.=009 **Significant Interaction Between Age and Time Frequent Cannabis Users**

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
Albertella, L. et al. (2018) Longitudinal Australia	Frequency of use past six months Frequency of use past month **Psychotic-Like Experiences Assessment** Adapted version of the short form of the Oxford-Liverpool Inventory of Feeling and Experiences		Past Month Cannabis Use (Changes of use overtime) Age Gender Family history of Psychosis Age of First Cannabis Use Age of First Alcohol Use Lifetime Unusual Experiences Score			B=0.31, p=.001 **Significant Interaction Between Age and Time Occasional Users** B=-0.02, p=.001 Among frequent cannabis users, younger age was associated with increasing levels of negative schizotypy over time. In contrast, among occasional users, younger age was associated with decreasing levels of negative schizotypy over time. Emerging human research is also pointing to negative emotionality as particularly affected by early onset cannabis use (Manza, Tomasi, & Volkow 2017).
12 **Age-Varying Effects of Cannabis Use Frequency and Disorder on Symptoms of Psychosis, Depression and Anxiety in Adolescents and Adults** Leadbeater, B. et al. (2018) Canada USA Adolescent Data Part Longitudinal (6 waves)	**Participants in Canada (Adolescents)** 662 Age range: 12-18 years old **Cannabis Use Assessment** Past year use (0= never to 4=more than once a week) **Cannabis Use Disorder Assessment** Mini-International Neuropsychiatric Interview **Psychotic-Like Experiences Assessment** Symptoms Checklist 90-Revised (SLC-90)	**Prevalence of Cannabis Use** Time 1 36% Time2 52% Time 3 61% Time 4 84% Time 5 72% Time 6 71%	Gender Socioeconomic Status Cigarette Use Alcohol Use Heavy Episodic Drinking	Time-Varying Effect Models flexibility estimates linear regressions	**NR**	**Frequent Cannabis Use and Psychotic Symptoms After Age 22** b=0.13, 95%CI=0.002-0.25 **Cannabis Use Disorder and Psychotic Symptoms After Age 23** b=0.51, 95%CI=0.01-1.01) **Significant Sex Differences between Cannabis Use Disorder and Psychotic-Symptoms** Interaction was significant following age 26 b=1.12, 95%CI=0.02-2.21 when females showed stronger associations than males

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Unstandardized Beta
Adult Data Cross-Sectional		**Prevalence of Psychotic-Like Experiences** NR				

9.3.3. Table 3. Studies Included in Systematic Review: Other Analyses

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Odds Ratio	Unstandardized Beta
1 **Cannabis Use Predicts Future Psychotic Symptoms and Vice-versa** Ferdinand, R. et al. (2005) Netherlands Cohort Study (Symptoms not Disorder) Longitudinal	**Participants** 2,076 participants 1,016 males 1,060 females **Cannabis Use Assessment** Composite International Diagnostic Interview (CIDI) **Psychotic-Like Experiences Assessment** Composite International Diagnostic Interview (CIDI) Lifetime symptoms	**Prevalence of Cannabis Use** 23.29% **Prevalence of Psychotic-Like Experiences** 10.44%	Age Gender	Cox Regression Analysis Survival time was defined in years, as age at onset of psychotic symptoms or if psychotic symptoms did not occur, as the age at the final assessment. Hazard ratios (HR) were computed that indicate the association between cannabis use and future psychotic symptoms. Proportional hazards assumption was tested for the time-dependent covariate by testing its interaction with time (age).	**Significant Association Between Life-Time Psychotic Symptoms and Life-Time Cannabis Use** x2 = 22.9 p < 0.001 k = 0.11 p < 0.001 Cannabis use and psychotic-symptoms absent: 1110 Cannabis use absent and psychotic symptoms present: 102 Cannabis use present and psychotic symptoms absent: 305 Cannabis use present and psychotic symptoms present: 63	**Cannabis Use Predicted Psychotic Symptoms** Hazard Ratio (95%) 2.81 (1.79 – 4.43) Risk of future psychotic symptoms in cannabis users increased almost threefold **Minimum Period of 2 Years Between Cannabis Use and Onset of Psychotic Symptoms** Hazard Ratio (95%) 2.07 (1.20 – 3.57)	**NR**
2 **Cannabis-Psychosis Pathway Independent of Other Types of Psychopathology** Ferdinand, R. et al. (2005)	**Participants** 2,076 participants 1,016 males 1,060 females **Cannabis Use Assessment** Composite International Diagnostic Interview (CIDI)	**Prevalence of Cannabis Use** 23.29% **Prevalence of Psychotic-Like Experiences** 10.44%	Age Gender	Cox Regression Analyses: In the first set of analyses it was determined whether cannabis use increased the risk for psychotic-symptoms and if this risk occurred independently of the other types of psychopathology Survival Analyses with cannabis use and each of the 8	Analysis Continuation Proportional Hazard Assumption was tested for the time-dependent covariate for each of the CBCL syndrome scores by testing interactions with time (age)	Cannabis use remained a significant predictor of psychotic symptoms even in the presence of other putative predictors such as Time 1 psychopathology scores	**NA**

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Odds Ratio	Unstandardized Beta
Netherlands Cohort Study (Symptoms not Disorder) <u>Same Study as Above</u>	**Psychotic-Like Experiences Assessment** Composite International Diagnostic Interview (CIDI) Lifetime symptoms Child Behaviour Checklist to Assess Further Psychopathology			CBCL syndrome scale scores separately as candidate predictors Survival time was defined in years as age of onset of psychotic symptoms or if these did not occur as the age at final assessment Hazard Ratios to indicate the association between cannabis use and future psychotic symptoms Cannabis use was entered as a time dependent covariate Possible cohort effects were adjusted for by fitting stratified Cox Regressions			
3 **Cannabis Use, Psychotic-Like Experiences and Aberrant Salience in a Sample of Belgian Students** Bernardini, F. et al. (2018) Brussels Cross-Sectional	**Participants** 257 Undergraduate Students **Cannabis Use Assessment** Lifetime and current cannabis use **Psychotic-Like Experiences Assessment** Aberrant Salience Inventory (ASI)	**Prevalence of Cannabis Use** Lifetime Use 46.3% Current Use 35% **Prevalence of Psychotic-Like Experiences** NR	Age Gender SES Financial support Part-time worker	Spearman Correlation Test Multivariate Econometric Linear Regression Model to test for significance of correlation between cannabis use and psychotic-like experiences Mann-Whitney U Test	**NR** Cannabis users showed significant higher ASI scores and higher positive and negative dimensions CAPE scores than non-users. Years of cannabis use and frequency of use in the last 30 days showed a small positive correlation with ASI scores. Weaker positive correlations with CAPE positive and negative dimensions score were observed.	**NR**	**<u>ASI and cannabis use</u>** is highly statistically significant in all regressions even after controlling for individuals' observables (244) **No. of years use** 1.171, R^2=0.07, p<0.01 **No. of years use + controls** 1.270, R^2=0.11, p<0.01 **No. days use in last 30** 1.264, R^2=0.07, p<0.01 **No. days use in last 30 + controls** 1.377, R^2=0.12, p<0.01 **Quantity use in last 30**

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Odds Ratio	Unstandardized Beta
	Assessment of Psychic Experiences (CAPE)						5.382, R^2=0.12, p<0.01 **Quantity use in last 30 + controls** 5.581, R^2=0.17, p<0.01 **<u>CAPE and cannabis use</u>** are significant in all regressions even after controlling **No. of years use** 0.032, R^2=0.02, p<0.05 **No. of years use + controls** 0.029, R^2=0.09, p<0.1 **No. days use in last 30** 0.033, R^2=0.02, p<0.01 **No. days use in last 30 + controls** 0.027, R^2=0.09, p<0.05 **Quantity use in last 30** 0.155, R^2=0.04, p<0.01 **Quantity use in last 30 + controls** 0.149, R^2=0.11, p<0.01 **CAPE positive and negative dimensions,** the correlations remained highly significant after controlling for individual characteristics when considering the quantity of cannabis consumed in the last 30 days **Positive Dimension** **No. of years use** 0.039, R^2=0.04, p<0.01 **No. of years use + controls** 0.029, R^2=0.11, p<0.05

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Odds Ratio	Unstandardized Beta
							No. days use in last 30 0.037, R^2=0.03, p<0.01 **No. days use in last 30 + controls** 0.023, R^2=0.10, p=not sig **Quantity use in last 30** 0.167, R^2=0.06, p<0.01 **Quantity use in last 30 + controls** 0.139, R^2=0.13, p<0.01 **Negative Dimension** **No. days use in last 30** 0.040, R^2=0.01, p<0.05 **No. days use in last 30 + controls** 0.042, R^2=0.05, p<0.1 **Quantity use in last 30** 0.186, R^2=0.03, p<0.05 **Quantity use in last 30 + controls** 0.230, R^2=0.07, p<0.05
4 **Psychotic-Like Experiences and Cannabis Use in Adolescents from the General Population** Fonseca-Pedrero, E. et al. (2019) Spain	**Participants** 1,588 **Age Range** 14 to 19 years old **Cannabis Use Assessment** Modified Substance Use Questionnaire (Abbreviated Assist) **Psychotic-Like Experiences Assessment**	**Prevalence of Cannabis Use** 23.7% **Prevalence of Psychotic-Like Experiences** 27.3%	Gender Age Socioeconomic Level Smoking Alcohol Use IQ	Multivariate Analysis of Variance (MANOVA) Chi-Square Analysis Partial eta Squared foe Effect Size Mediation Analysis Sobel Test to verify the significance of the possible indirect effect	**NR**	**NA**	Relationship between PQ-B and Cannabis Use (MANOVA) λ=0.994 F(2,1585)=5.049 p=0.007 Frequency and distress associated with psychotic-like experiences among cannabis users increased Psychosis Risk Groups and Cannabis Use $X^2_{(1)}$=8.450, p=0.004 MANCOVA

Author / Country / Study Design	Participants / Cannabis Use Assessment / Psychotic-Like Experiences Assessment	Prevalence of Cannabis Use / Prevalence of Psychotic-Like Experiences	Covariates	Analysis	Est. Effect Size	Odds Ratio	Unstandardized Beta
Cross-sectional	Prodromal Questionnaire-Brief (PB-Q)		Emotional Behaviour Problems				PQ-B as dependent variable, Cannabis as fixed factor controlling for covariates showed absence of statistically significant differences between groups $\lambda=0.999$, $F(1,1580)=0.523$, $p=0.593$